Supporting Information

C3-Hetero-functionalization of Indole Derivatives via Facilitated Indolyl 1,3-Heteroatom Transposition

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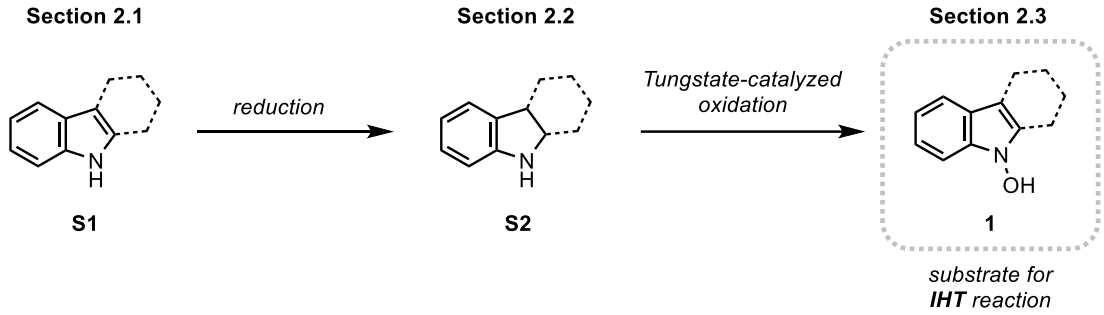
1. General Information

Reactions were performed in oven-dried or flame-dried glassware under N_2 atmosphere with dry solvents under anhydrous conditions, unless otherwise stated. Tetrahydrofuran (THF) and dichloromethane (CH_2Cl_2) were initially degassed by sonication, and subsequently dried by passing them through a PureSolv solvent purification system and toluene was dried over CaH_2 and distilled under N_2 atmosphere. *N,N*-Dimethylformamide (DMF), dimethyl sulfoxide (DMSO), 1,2-dichloroethane (DCE), acetonitrile (MeCN), and 1,4-dioxane were purchased in anhydrous form from a commercial source (Sigma-Aldrich). Nitromethane was dried over molecular sieves (4Å) and degassed prior to use. Acetone, ethyl acetate (EtOAc), diethyl ether (Et_2O), CH_2Cl_2, hexanes, and water (H_2O) were purchased from a commercial source (Samchun Chemical) and used without further purification. $H_2{}^{18}O$ (97 atom% ^{18}O) was purchased from Sigma-Aldrich and used as received. Other reagents were purchased from commercial sources (Sigma-Aldrich, Alfa Aesar, Acros Organics, and TCI) and used as received. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layers chromatography (TLC) using 0.25 mm E. Merck silica gel plates (60 F_{254}) and the developed chromatogram was visualized by using UV light or an acidic ethanolic anisaldehyde or potassium permanganate ($KMnO_4$) stain with heating. Intertec Silica gel (60, particle size 60–200 μm) was used for flash column chromatography. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on an Agilent 400-MR DD2 Magnetic Resonance System, Varian/Oxford As-500 instrument, or Bruker 500 MHz instrument and calibrated using residual un-deuterated solvent signal ($CHCl_3$ in $CDCl_3$: δ 7.26 ppm for ^{1}H, δ 77.16 ppm for ^{13}C; CH_3OH in MeOD: δ 3.31 ppm for ^{1}H, δ 49.00 ppm for ^{13}C) as the internal reference. ^{19}F NMR spectra were calibrated to an external standard of neat $PhCF_3$ (δ –63.72 ppm). Data for NMR spectra were reported as follows: chemical shift (multiplicities, coupling constant (Hz), and integration) and chemical shifts are reported in ppm. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, qui = quintet, h = heptet, dd = doublet of doublets, dq = doublet of quartets, dm = doublet of multiplets, td = triplet of doublets, tt = triplet of triplets, qd = quartet of doublets, ddd = doublet of doublet of doublets, dddd = doublet of doublet of doublet of doublets, ddt = doublet of doublet of triplets, dtd = doublet of triplet of doublets, dtt= doublet of triplet of triplets, tdd = triplet of doublet of doublets, m = multiplet, br = broad. High-resolution mass spectrometry (HRMS) was performed using a HRMS-ESI Q-TOF 5600 spectrometer at National Instrumentation

Center for Environmental Management (NICEM) in Seoul National University, Ultra High Resolution ESI Q-TOF mass spectrometer (Bruker compact) at the Organic Chemistry Research Center in Sogang University, or ThermoFisher Scientific mass spectrometer (Orbitrap Exploris 120) at Department of Chemistry in Seoul National University.

2. Preparation of Starting Materials

Scheme S1. Synthetic scheme for the preparation of *N*-hydroxyindole **1**.



The synthetic scheme for the preparation of *N*-hydroxyindole **1**, the substrate of indolyl 1,3-heteroatom transposition (**IHT**) reaction, is depicted in Scheme **S1**. The two-step sequence, reduction of indole **S1** followed by tungstate-catalyzed oxidation, was utilized to provide a series of *N*-hydroxyindole **1.**[1] Detailed information on the preparation and characterization of **S1**, **S2** and **1** is described in Section **2.1**, **2.2** and **2.3**, respectively.

2.1. Preparation of Indole Derivatives

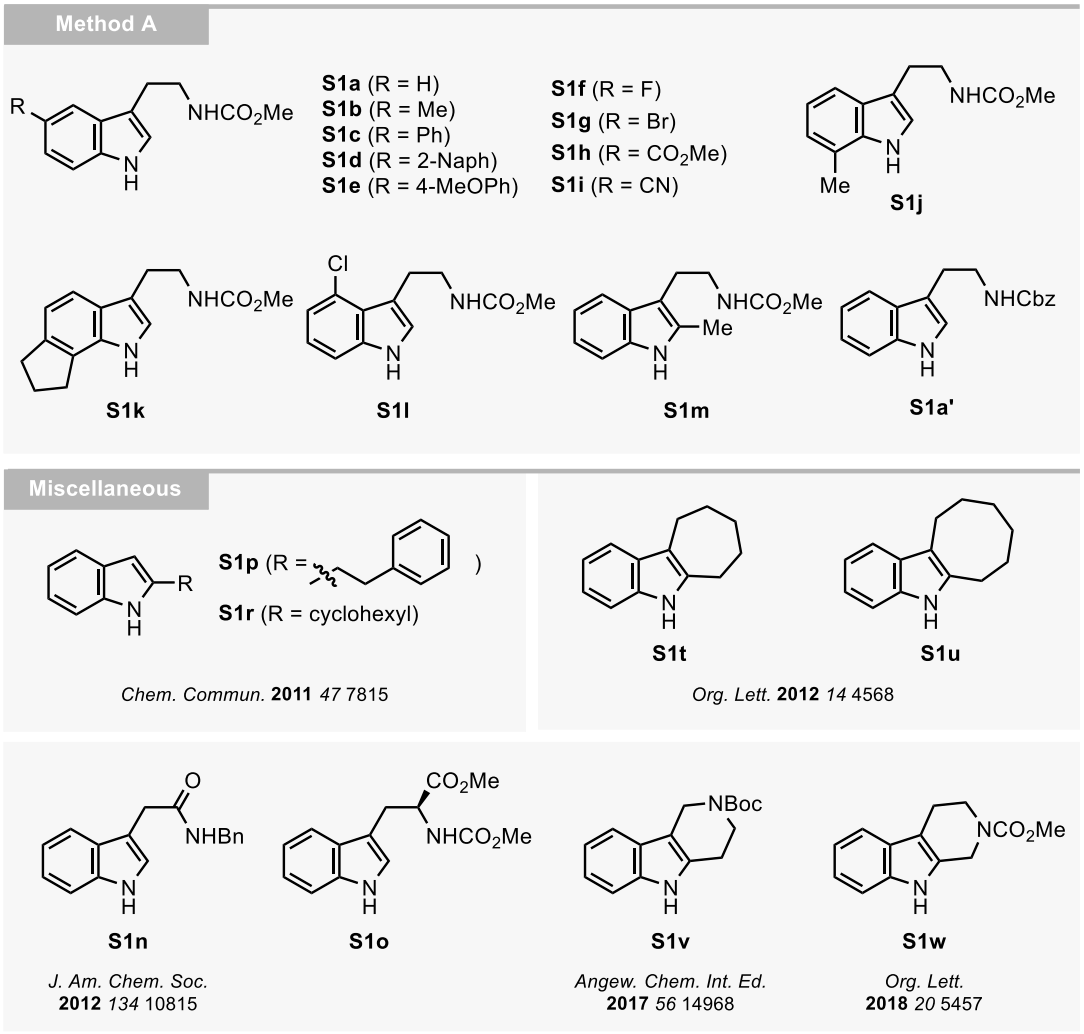
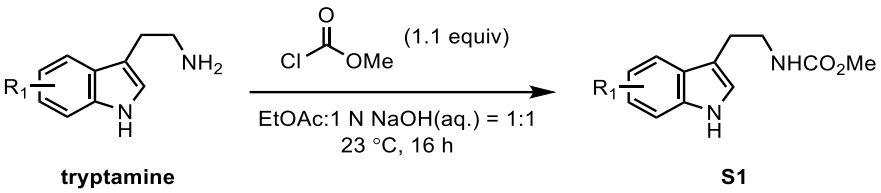


Figure S1. List of indole derivatives categorized by methods of preparation.

The spectral data matched to those reported in the literature: S1a[2], S1b[2], S1f[2], S1g[3], S1j[3], S1l[2], S1m[4], S1n[5], S1o, S1p[6], S1r[6], S1t[7], S1u[7], S1v[8], S1w[9], S1a[10].

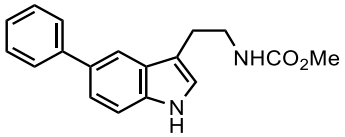
General procedure A



tryptamine **S1**

To an oven-dried round-bottom flask equipped with a stir bar and septum were added tryptamine (1.0 equiv) and EtOAc:1 N NaOH (1:1, 0.2 M in tryptamine) at 23 °C, followed by methyl chloroformate (1.1 equiv). The resulting mixture was stirred for 16 h, before it was quenched with H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the desired product.

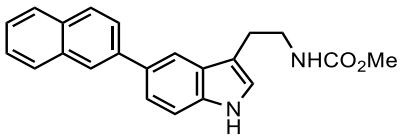
Methyl (2-(5-phenyl-1H-indol-3-yl)ethyl)carbamate (S1c)



Following the **general procedure A**, 5-phenyl tryptamine (0.580 g, 1.97 mmol) afforded tryptamine **S1c** (465 mg, 80%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.40 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.42 (br s, 1H), 7.84 (s, 1H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.51 – 7.47 (m, 3H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.06 – 6.96 (m, 1H), 4.94 (br s, 1H), 3.70 (s, 3H), 3.60 – 3.55 (m, 2H), 3.03 (t, *J* = 6.8 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.3, 142.5, 135.9, 132.8, 128.7, 127.8, 127.3, 126.3, 123.0, 121.7, 117.0, 112.9, 111.6, 52.0, 41.5, 25.6; **HRMS** calcd. for $C_{18}H_{19}N_2O_2^+$ $[M + H]^+$ 295.1441, found 295.1438.

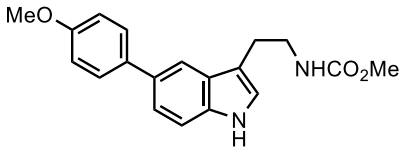
Methyl (2-(5-(naphthalen-2-yl)-1H-indol-3-yl)ethyl)carbamate (S1d)



Following the **general procedure A**, 5-(naphthalen-2-yl)-tryptamine (0.490 g, 1.71 mmol) afforded tryptamine **S1d** (0.340 g, 58%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.40 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.11 (br s, 1H), 8.09 (s, 1H), 7.94 – 7.90 (m, 3H), 7.88 – 7.83 (m, 2H), 7.60 (d, *J* = 8.3 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.09 (s, 1H), 4.80 (s, 1H), 3.67 (s, 3H), 3.58 (br q, *J* = 6.5 Hz, 2H), 3.05 (t, *J* = 6.8 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.2, 139.9, 136.1, 134.0, 133.1, 132.3, 128.4, 128.2, 128.1, 127.8, 126.4, 126.3, 125.7, 125.6, 123.0, 122.4, 117.7, 113.5, 111.7, 52.2, 41.5, 25.9; **HRMS** calcd. for $C_{22}H_{21}N_2O_2^+$ $[M + H]^+$ 345.1598, found 345.1591.

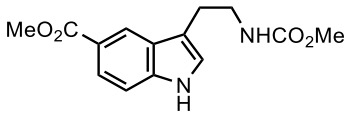
Methyl (2-(5-(4-methoxyphenyl)-1H-indol-3-yl)ethyl)carbamate (S1e)



Following the **general procedure A**, 5-(4-methoxyphenyl)-tryptamine (0.750 g, 2.82 mmol) afforded tryptamine **S1e** (0.630 g, 69%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.27 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.15 (br s, 1H), 7.74 (s, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.04 (s, 1H), 7.00 (d, *J* = 8.6 Hz, 2H), 4.81 (br s, 1H), 3.87 (s, 3H), 3.67 (s, 3H), 3.57 – 3.53 (m, 2H), 3.01 (t, *J* = 6.8 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 158.6, 157.2, 135.7, 135.3, 133.0, 128.5, 128.0, 122.9, 12.0, 116.9, 114.3, 113.4, 111.5, 55.5, 52.2, 41.5, 25.9; **HRMS** calcd. for $C_{19}H_{21}N_2O_3^+$ $[M + H]^+$ 325.1547, found 325.1556.

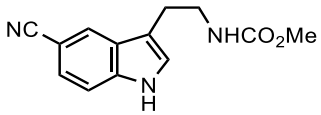
Methyl 3-(2-((methoxycarbonyl)amino)ethyl)-1H-indole-5-carboxylate (S1h)



Following the **general procedure A**, Methyl tryptamine-5-carboxylate (0.300 g, 1.36 mmol) afforded tryptamine **S1h** (0.210 g, 56%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

***R*$_f$**=0.40 (silica gel, hexanes:EtOAc = 4:6); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.78 (br s, 1H), 8.35 (s, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 7.06 (s, 1H), 4.88 (br s, 1H), 3.93 (s, 3H), 3.65 (s, 3H), 3.53 – 3.48 (m, 2H), 2.97 (t, *J* = 6.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 168.4, 157.3, 139.1, 127.0, 123.6, 123.5, 121.7, 121.4, 114.3, 111.1, 52.2, 52.0, 41.4, 25.7; **HRMS** calcd. for $C_{14}H_{17}N_2O_4^+$ $[M + H]^+$ 277.1187, found 277.1182.

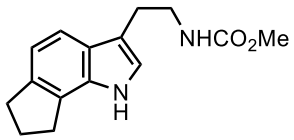
Methyl (2-(5-cyano-1H-indol-3-yl)ethyl)carbamate (S1i)



Following the **general procedure A**, 5-cyanotryptamine (352 mg, 1.88 mmol) afforded tryptamine **S1i** (0.250 g, 55%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

***R*$_f$**=0.20 (silica gel, hexanes:EtOAc = 4:6); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.58 (br s, 1H), 7.94 (s, 1H), 7.42 (s, 2H), 7.16 (s, 1H), 4.81 (br s, 1H), 3.67 (s, 3H), 3.53 – 3.48 (m, 2H), 2.97 (t, *J* = 6.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.2, 138.1, 127.4, 125.2, 124.6, 124.3, 120.9, 114.2, 112.3, 102.7, 52.3, 41.4, 25.7; **HRMS** calcd. for $C_{13}H_{14}N_3O_2^+$ $[M + H]^+$ 244.1076, found 244.1081.

Methyl (2-(1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)ethyl)carbamate (S1k)



Following the **general procedure A**, 2-(1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)ethan-1-amine (0.230 g, 1.14 mmol) afforded tryptamine **S1k** (191 mg, 65%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.60 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.93 (br s, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.97 (s, 1H), 4.77 (br s, 1H), 3.66 (s, 3H), 3.52 (d, *J* = 6.6 Hz, 2H), 3.05 (q, *J* = 8.0 Hz, 4H), 2.97 (t, *J* = 6.9 Hz, 2H), 2.22 (p, *J* = 7.3 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.2, 138.9, 133.7, 126.0, 125.7, 121.4, 116.9, 116.6, 113.6, 52.1, 41.4, 33.2, 29.9, 26.1, 25.5; **HRMS** calcd. for $C_{15}H_{20}N_2O_2^+$ $[M + H]^+$ 259.1441, found 259.1439.

2.2. Preparation of Indoline Derivatives

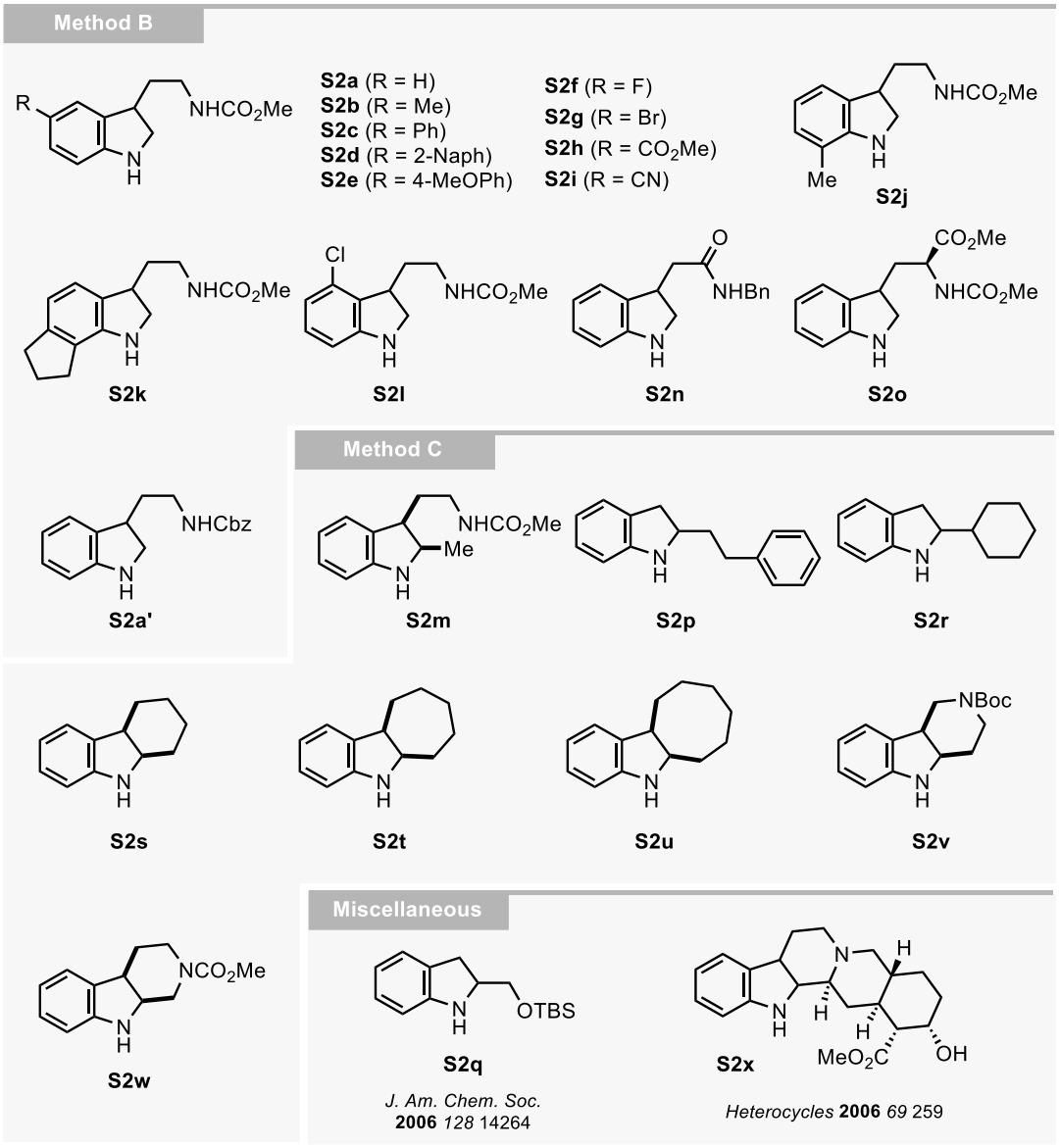
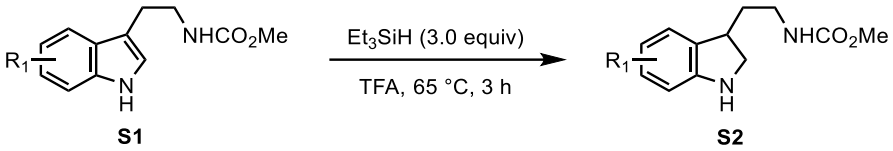


Figure S2. List of indoline derivatives categorized by methods of preparation.

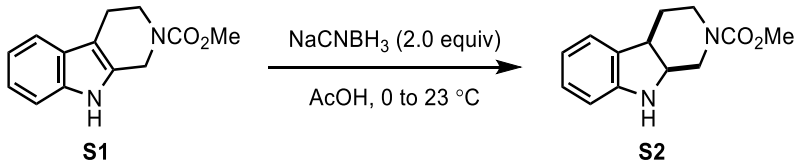
The spectral data matched to those reported in the literature: S2p[11], S2q[11], S2r[12], S2s[11], S2t[11], S2u[13], S2x[1]

General procedure B



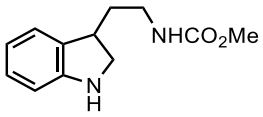
To an oven-dried round-bottom flask equipped with a stir bar and septum were added indole **S1** (1.0 equiv) and TFA (0.3 M in **S1**) at 23 °C, followed by Et_3SiH (3.0 equiv). The resulting mixture was heated to 65 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to remove most of TFA. The crude product was re-dissolved in CH_2Cl_2 and basified to pH 9−10 using $NH_3·H_2O$ (25.0−30.0 wt% in H_2O). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford indoline **S2**.

General procedure C



To an oven-dried round-bottom flask equipped with a stir bar and septum were added indole **S1**(1.0 equiv) and AcOH (0.1 M in **S1**) at 23 °C. The resulting solution was cooled to 0 °C, and $NaBH_3CN$ (2.0 equiv) was added to the solution. The reaction mixture was warmed up to 23 °C and stirred while the reaction was monitored by TLC. After completion of reaction (1−2 h), the reaction mixture was directly concentrated under reduced pressure. The crude product was re-dissolved in CH_2Cl_2 and basified to pH 9−10 using $NH_3·H_2O$ (25.0−30.0 wt% in H_2O). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford indoline **S2**.

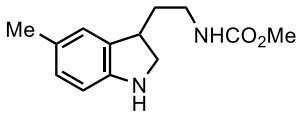
Methyl (2-(indolin-3-yl)ethyl)carbamate (S2a)



Following the **general procedure B**, tryptamine **S1a** (3.50 g, 16.0 mmol) afforded indoline **S2a** (3.30 g, 94%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

R_f=0.20 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.08 (d, *J* = 7.3 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 7.7 Hz, 1H), 5.03 (s, 1H), 3.78 – 3.62 (m, 5H), 3.35 – 3.26 (m, 2H), 3.22 (m, 2H), 2.04 – 1.93 (m, 1H), 1.73 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.2, 151.3, 132.1, 127.7, 123.9, 118.8, 109.7, 53.3, 52.1, 39.6, 39.1, 34.5; **HRMS** calcd. for $C_{12}H_{17}N_2O_2^+$ $[M + H]^+$ 221.1285, found 221.1278.

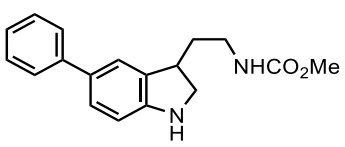
Methyl (2-(5-methylindolin-3-yl)ethyl)carbamate (S2b)



Following the **general procedure B**, tryptamine **S1b** (0.100 g, 0.431 mmol) afforded indoline **S2b** (75.0 mg, 74%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

R_f=0.34 (silica gel, hexanes:EtOAc = 4:6); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.91 (s, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 6.57 (d, *J* = 7.8 Hz, 1H), 4.86 (br s, 1H), 3.68 (t, *J* = 7.3 Hz, 2H), 3.66 (s, 3H), 3.35 – 3.18 (m, 4H), 2.26 (s, 3H), 2.04 – 1.95 (m, 1H), 1.78 – 1.69 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.2, 148.8, 132.5, 128.1, 127.9, 124.5, 109.7, 53.4, 51.9, 39.5, 39.0, 34.3, 20.8; **HRMS** calcd. for $C_{13}H_{19}N_2O_2^+$ $[M + H]^+$ 235.1442, found 235.1441.

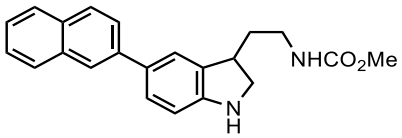
Methyl (2-(5-phenylindolin-3-yl)ethyl)carbamate (S2c)



Following the **general procedure B**, tryptamine **S1c** (0.300 g, 1.02 mmol) afforded indoline **S2c** (0.265 g, 88%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

R_f=0.30 (silica gel, hexanes:EtOAc = 4:6); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.7 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.34 (s, 1H), 7.33 – 7.27 (m, 2H), 6.71 (d, *J* = 8.0 Hz, 1H), 5.01 (br s, 1H), 3.75 (t, *J* = 8.7 Hz, 1H), 3.68 (s, 3H), 3.41 – 3.35 (m, 1H), 3.33 – 3.24 (m, 3H), 2.09 – 2.03 (m, 1H), 1.79 (dt, *J* = 14.2, 7.1 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.2, 150.7, 141.6, 132.9, 132.2, 128.7, 126.8, 126.6, 126.2, 122.8, 109.8, 53.5, 52.1, 39.5, 39.1, 34.6; **HRMS** calcd. for $C_{18}H_{21}N_2O_2^+$ $[M + H]^+$ 297.1592, found 297.1598.

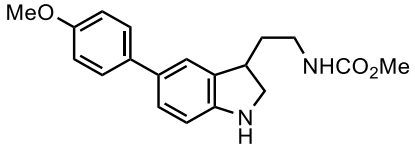
Methyl (2-(5-(naphthalen-2-yl)indolin-3-yl)ethyl)carbamate (S2d)



Following the **general procedure B**, tryptamine **S1d** (0.450 g, 1.31 mmol) afforded indoline **S2d** (0.330 g, 73%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

R_f=0.33 (silica gel, hexanes:EtOAc = 4:6); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.71 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.52 – 7.40 (m, 4H), 6.74 (d, *J* = 8.0 Hz, 1H), 4.92 (s, 1H), 3.77 (t, *J* = 8.7 Hz, 1H), 3.68 (s, 3H), 3.45 – 3.37 (m, 1H), 3.37 – 3.24 (m, 3H), 2.15 – 2.03 (m, 1H), 1.88 – 1.76 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.3, 150.9, 139.1, 134.0, 133.0, 132.2, 132.0, 128.3, 128.0, 127.7, 127.2, 126.2, 125.6, 125.5, 124.6, 123.1, 109.9, 53.5, 52.2, 39.7, 39.2, 34.7; **HRMS** calcd. for $C_{22}H_{23}N_2O_2^+$ $[M + H]^+$ 347.1754, found 347.1748.

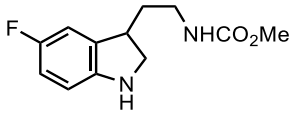
Methyl (2-(5-(4-methoxyphenyl)indolin-3-yl)ethyl)carbamate (S2e)



Following the **general procedure B**, tryptamine **S1e** (0.370 g, 1.14 mmol) afforded indoline **S2e** (0.280 g, 75%)

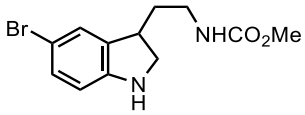
as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4). R_f=0.10 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 6.5 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 2H), 6.61 (d, *J* = 8.0 Hz, 1H), 5.33 (br s, 1H), 3.85 (s, 1H), 3.77 (s, 3H), 3.64 (s, 3H), 3.32 – 3.12 (m, 4H), 2.02 – 1.96 (m, 1H), 1.73 – 166 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 158.1, 157.1, 150.2, 134.1, 132.7, 131.3, 127.2, 126.0, 122.1, 113.9, 109.5, 55.1, 53.2, 51.8, 39.3, 38.9, 34.2; **HRMS** calcd. for $C_{19}H_{23}N_2O_3^+$ $[M + H]^+$ 327.1701, found 327.1703.

Methyl (2-(5-fluoroindolin-3-yl)ethyl)carbamate (S2f)



Following the **general procedure B**, tryptamine **S1f** (1.80 g, 7.62 mmol) afforded indoline **S2f** (1.30 g, 72%) as a brown oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1). R_f=0.28 (silica gel, hexanes:EtOAc = 2:8); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.81 (d, *J* = 8.3 Hz, 1H), 6.73 (t, *J* = 8.8 Hz, 1H), 6.54 (dd, *J* = 8.5, 4.3 Hz, 1H), 4.88 (br s, 1H), 3.71 (t, *J* = 8.0 Hz, 2H), 3.66 (s, 3H), 3.35 – 3.17 (m, 4H), 2.03 – 1.90 (m, 1H), 1.79 – 1.68 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.2 (d, *J* = 235.6 Hz), 157.2, 147.3 (d, *J* = 1.4 Hz), 134.0 (d, *J* = 6.1 Hz), 113.8 (d, *J* = 23.4 Hz), 111.4 (d, *J* = 23.9 Hz), 110.0 (d, *J* = 8.2 Hz), 53.9, 52.2, 40.0, 39.0, 34.4; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −126.1; **HRMS** calcd. for $C_{12}H_{16}FN_2O_2^+$ $[M + H]^+$ 239.1188, found 239.1190.

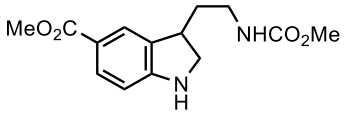
Methyl (2-(5-bromoindolin-3-yl)ethyl)carbamate (S2g)



Following the **general procedure B**, tryptamine **S1g** (0.500 g, 1.68 mmol) afforded indoline **S2g** (0.400 g, 80%) as a yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1).

***R**f*=0.23 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.16 (s, 1H), 7.12 (d, *J* = 7.9 Hz, 1H), 6.50 (d, *J* = 8.2 Hz, 1H), 4.80 (br s, 1H), 3.75 – 3.65 (m, 4H), 3.36 – 3.20 (m, 4H), 2.01 – 1.93 (s, 1H), 1.80 – 1.69 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.2, 150.4, 134.6, 130.4, 127.0, 110.9, 110.3, 53.5, 52.2, 39.6, 39.0, 34.5; **HRMS** calcd. for $C_{12}H_{16}BrN_2O_2^+$ $[M + H]^+$ 299.0390, found 299.0390.

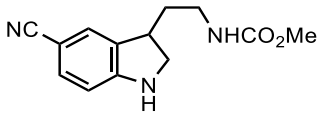
Methyl 3-(2-((methoxycarbonyl)amino)ethyl)indoline-5-carboxylate (S2h)



Following the **general procedure B**, tryptamine **S1h** (0.340 g, 1.23 mmol) afforded indoline **S2h** (0.212 g, 76%) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1).

***R**f*=0.45 (silica gel, hexanes:EtOAc = 2:8); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.78 (s, 1H), 8.35 (s, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 7.06 (s, 1H), 4.88 (s, 1H), 3.93 (s, 3H), 3.65 (s, 3H), 3.57 – 3.42 (m, 2H), 2.97 (t, *J* = 6.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 168.4, 157.3, 139.1, 127.0, 123.6, 123.5, 121.8, 121.4, 114.3, 111.1, 52.2, 52.0, 41.4, 25.7; **HRMS** calcd. for $C_{14}H_{19}N_2O_4^+$ $[M + H]^+$ 279.1341, found 279.1339.

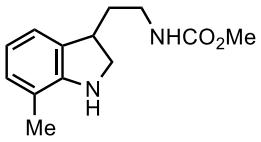
Methyl (2-(5-cyanoindolin-3-yl)ethyl)carbamate (S2i)



Following the **general procedure B**, tryptamine **S1i** (0.900 g, 3.70 mmol) afforded indoline **S2i** (0.700 g, 77%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1).

***R**f*=0.34 (silica gel, hexanes:EtOAc = 2:8); **^{1}H NMR** (400 MHz, MeOD): δ 7.33 – 7.26 (m, 2H), 6.54 (d, *J* = 8.2 Hz, 1H), 3.79 – 3.72 (m, 1H), 3.63 (s, 3H), 3.35 – 3.27 (m, 2H), 3.19 (t, *J* = 7.6 Hz, 2H), 1.97 – 1.90 (m, 1H), 1.75 – 1.65 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.3, 155.1, 133.5, 132.6, 127.6, 120.8, 108.4, 99.7, 53.0, 52.3, 38.8, 38.7, 34.8; **HRMS** calcd. for $C_{13}H_{16}N_3O_2^+$ $[M + H]^+$ 246.1234, found 246.1237.

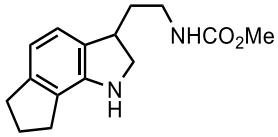
Methyl (2-(7-methylindolin-3-yl)ethyl)carbamate (S2j)



Following the **general procedure B**, tryptamine **S1j** (0.450 g, 1.94 mmol) afforded indoline **S2j** (0.345 g, 76%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

R_f=0.34 (silica gel, hexanes:EtOAc = 2:8); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.96 (d, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.69 (t, *J* = 7.4 Hz, 1H), 4.91 (br s, 1H), 3.76 – 3.69 (m, 2H), 3.67 (s, 2H), 3.39 – 3.30 (m, 1H), 3.30 – 3.17 (m, 3H), 2.13 (s, 3H), 2.06 – 1.93 (m, 1H), 1.81 – 1.68 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.2, 149.8, 131.5, 128.7, 121.5, 119.3, 119.1, 53.2, 52.2, 40.0, 39.2, 34.7, 16.9; **HRMS** calcd. for $C_{13}H_{19}N_2O_2^+$ $[M + H]^+$ 235.1441, found 235.1441.

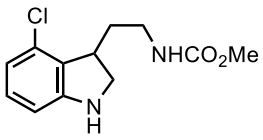
Methyl (2-(1,2,3,6,7,8-hexahydrocyclopenta[g]indol-3-yl)ethyl)carbamate (S2k)



Following the **general procedure B**, tryptamine **S1k** (0.230 g, 0.891 mmol) afforded indoline **S2k** (0.210 g, 91%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

R_f=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.91 (d, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 7.4 Hz, 1H), 4.83 (br s, 1H), 3.73 (t, *J* = 8.2 Hz, 1H), 3.67 (s, 3H), 3.57 (s, 1H), 3.37 – 3.15 (m, 4H), 2.86 (t, *J* = 7.5 Hz, 2H), 2.70 (t, *J* = 7.3 Hz, 2H), 2.17 (s, 1H), 2.08 (p, *J* = 7.5 Hz, 2H), 1.99 (dq, *J* = 13.9, 7.0 Hz, 1H), 1.74 (dq, *J* = 14.4, 7.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.2, 147.3, 144.8, 129.7, 125.2, 121.9, 114.8, 77.4, 77.2, 76.9, 53.9, 52.2, 39.7, 39.3, 34.9, 32.9, 31.1, 29.5, 25.6; **HRMS** calcd. for $C_{15}H_{21}N_2O_2^+$ $[M + H]^+$ 261.1598, found 261.1590.

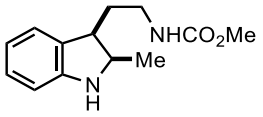
Methyl (2-(4-chloroindolin-3-yl)ethyl)carbamate (S2l)



Following the **general procedure B**, tryptamine **S1l** (0.100 g, 0.396 mmol) afforded indoline **S2l** (80.0 mg, 89%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1).

***R**f*=0.34 (silica gel, hexanes:EtOAc = 2:8); **^{1}H NMR** (400 MHz, $CDCl_3$):) δ 6.95 (t, *J* = 7.9 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 7.8 Hz, 1H), 4.97 (s, 1H), 3.87 (s, 1H), 3.68 (d, *J* = 8.8 Hz, 1H), 3.65 (s, 3H), 3.51 – 3.34 (m, 2H), 3.31 – 3.07 (m, 2H), 2.00 – 1.81 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.2, 152.8, 130.8, 129.6, 129.4, 119.1, 107.9, 77.5, 77.2, 76.8, 52.2, 52.1, 39.3, 38.7, 32.6; **HRMS** calcd. for $C_{12}H_{16}ClN_2O_2^+$ $[M + H]^+$ 255.0895, found 255.0892.

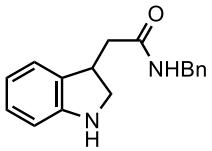
Methyl (2-(2-methylindolin-3-yl)ethyl)carbamate (S2m)



Following the **general procedure C** for 1 h, tryptamine **S1m** (0.500 g, 2.15 mmol) afforded indoline **S2m** (0.430 g, 85%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1).

***R**f*=0.48 (silica gel, hexanes:EtOAc = 2:8); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.09 – 7.04 (m, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.70 (q, *J* = 6.9 Hz, 1H), 6.59 (t, *J* = 8.7 Hz, 1H), 5.09 (br s, 1H), 3.95 and 3.59 (t, *J* = 6.1 Hz, 1H), 3.80 – 3.70 (m, 1H), 3.65 (s, 3H), 3.23 – 3.18 (m, 2H), 3.10 and 2.84 (q, *J* = 6.2 Hz, 1H), 1.91 – 1.73 (m, 2H), 1.22 and 1.16 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.2, 150.4, 150.0, 131.8, 131.3, 127.7, 127.5, 124.3, 124.3, 118.6, 118.5, 109.6, 109.4, 60.4, 58.3, 52.0, 47.1, 42.2, 39.3, 38.7, 34.3, 28.4, 22.2, 16.0; **HRMS** calcd. for $C_{13}H_{19}N_2O_2^+$ $[M + H]^+$ 235.1442, found 235.1441.

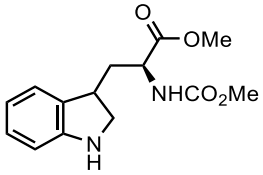
***N*-benzyl-2-(indolin-3-yl)acetamide (S2n)**



Following the **general procedure B**, indole **S1n** (2.30 g, 8.70 mmol) afforded indoline **S2n** (1.37 g, 59%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

***R*$_f$**=0.26 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.36 – 7.27 (m, 3H), 7.26 – 7.21 (m, 2H), 7.07 (d, *J* = 7.6 Hz, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 6.34 (s, 1H), 5.12 (s, 1H), 4.40 (d, *J* = 5.8 Hz, 2H), 3.80 – 3.74 (m, 1H), 3.70 (t, *J* = 9.0 Hz, 1H), 3.30 – 3.22 (m, 1H), 2.50 (ddd, *J* = 61.3, 14.5, 7.3 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$ δ 171.4, 150.0, 138.2, 138.2, 132.1, 132.1, 128.7, 128.1, 127.8, 127.5, 124.3, 119.7, 110.6, 110.6, 52.8, 43.6, 41.2, 38.9; **HRMS** calcd. for $C_{17}H_{19}N_2O^+$ $[M + H]^+$ 267.1492, found 267.1491.

Methyl (2S)-3-(indolin-3-yl)-2-((methoxycarbonyl)amino)propanoate (S2o)

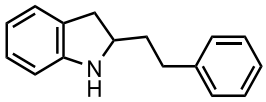


Following the **general procedure B**, tryptophan **S1o** (1.50 g, 5.43 mmol) afforded indoline **S2o** (1.07 g, 71%) as an inconsequential 1:1 mixture of diastereomers in the form of a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1). The resulting diastereomeric mixture was used directly in the subsequent reaction without separation. The diastereomeric ratio was determined by ^{1}H NMR analysis of the crude reaction mixture.

***R*$_f$**=0.25 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 50:50 mixture of diastereomers): δ 7.15 (d, *J* = 7.3 Hz, 0.5H), 7.05 (d, *J* = 7.3 Hz, 0.5H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.74 – 6.69 (m, 1H), 6.63 (t, *J* = 7.2 Hz, 1H), 5.61 (br s, 1H), 4.52 – 4.43 (m, 1H), 3.80-3.70 (m, 1H), 3.72 and 3.69 (s, 6H), 3.39 – 3.33 (m, 1H), 3.28 and 3.21 (t, *J* = 7.4 Hz, 1H), 2.29 and 1.87 (dt, *J* = 13.3, 6.1 Hz, 1H), 2.10 – 2.01 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 173.2, 156.9, 156.7, 151.2, 151.1, 131.7, 131.4, 127.9, 127.8, 124.3, 123.6, 118.9, 118.7, 109.8,

109.7, 53.7, 52.9, 52.6, 52.5, 52.4, 38.8, 38.6, 37.2; **HRMS** calcd. for $C_{14}H_{19}N_2O_4^+$ $[M + H]^+$ 279.1339, found 279.11340.

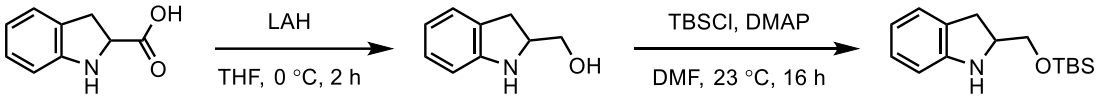
2-Phenethylindoline (S2p)



Following the **general procedure C** for 2 h, indole **S1p** (0.280 g, 1.27 mmol) afforded indoline **S2p** (0.230 g, 81%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.[11]

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.39 – 7.32 (m, 2H), 7.28 – 7.24 (m, 3H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.67 (t, *J* = 7.4 Hz, 1H), 6.61 (d, *J* = 7.7 Hz, 1H), 3.96 – 3.87 (m, 1H), 3.20 (dd, *J* = 15.4, 8.7 Hz, 1H), 2.80 – 2.73 (m, 3H), 2.03 – 1.97 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 151.0, 141.9, 128.8, 128.6, 128.4, 127.4, 126.1, 124.8, 118.7, 109.3, 59.6, 38.6, 36.2, 33.0.

2-(((*tert*-Butyldimethylsilyl)oxy)methyl)indoline (S2q)



Indoline-2-carboxylic acid **indolin-2-ylmethanol** **S2q**

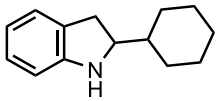
To an oven-dried round-bottom flask equipped with a stir bar and septum were added indoline-2-carboxylic acid (2.00 g, 12.3 mmol, 1.0 equiv) and THF (30 mL) at 23 °C. The resulting solution was cooled to 0 °C, and LAH (0.412 g, 13.7 mmol, 1.11 equiv) was added to the solution. The reaction mixture was stirred for 2 h before it was quenched with brine (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layer was washed with brine (3 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford crude indolin-2-ylmethanol, which was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added crude indolin-2-ylmethanol and DMF (20 mL) at 23 °C, followed by TBSCl (1.88 g, 12.5 mmol, 1.01 equiv) and DMAP (1.50 g, 12.3 mmol,

1.0 equiv). The resulting mixture was stirred for 16 h before it was quenched with brine (20 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was washed with brine (3 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5) to afford the product **S2q** (2.09 g, 73%) as a pale yellow oil. Analytic data is in agreement with the reported literature values.[11]

***R**f*=0.24 (silica gel, hexanes:EtOAc = 95:5); ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.10 (d, *J* = 7.3 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 7.7 Hz, 1H), 4.01 – 3.93 (m, 1H), 3.67 – 3.54 (m, 2H), 3.14 (dd, *J* = 15.8, 9.1 Hz, 1H), 2.68 (dd, *J* = 15.8, 5.8 Hz, 1H), 0.96 (s, 9H), 0.11 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.6, 128.2, 127.5, 124.9, 118.5, 109.4 5, 66.7, 60.5, 32.2, 26.0, 18.4, –5.2.

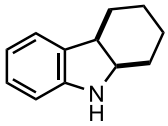
2-Cyclohexylindoline (S2r)



Following the **general procedure C** for 2 h, indole **S1r** (0.100 g, 0.502 mmol) afforded indoline **S2r** (82.0 mg, 81%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.[12]

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.08 (d, *J* = 7.3 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.68 (t, *J* = 7.4 Hz, 1H), 6.61 (d, *J* = 7.7 Hz, 1H), 3.94 (br s, 1H), 3.56 (q, *J* = 8.8 Hz, 1H), 3.07 (dd, *J* = 15.5, 8.7 Hz, 1H), 2.75 (dd, *J* = 15.5, 9.8 Hz, 1H), 1.89 (d, *J* = 12.3 Hz, 1H), 1.51 – 1.41 (m, 1H), 1.34 – 1.13 (m, 3H), 1.06 – 0.94 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 151.3, 129.2, 127.3, 124.6, 118.5, 109.0, 65.7, 44.0, 34.3, 30.3, 29.7, 26.6, 26.2, 26.1.

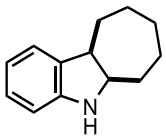
2,3,4,4a,9,9a-Hexahydro-1H-carbazole (S2s)



Following the **general procedure C** for 1 h, 1,2,3,4-tetrahydrocarbazole (3.00 g, 17.5 mmol) afforded indoline **S2s** (2.37 g, 78%) as a white amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.[11]

R_f=0.68 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.10 (d, *J* = 7.3 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.76 (t, *J* = 7.4 Hz, 1H), 6.69 (d, *J* = 7.7 Hz, 1H), 3.74 (q, *J* = 6.1 Hz, 1H), 3.11 (q, *J* = 6.7 Hz, 1H), 1.72 – 1.65 (m, 1H), 1.62 – 1.53 (m, 2H), 1.58 (dq, *J* = 12.5, 7.0, 5.5 Hz, 2H), 1.48 – 1.32 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 150.9, 133.9, 127.1, 123.3, 118.9, 110.3, 59.8, 41.1, 29.3, 27.1, 22.7, 21.8.

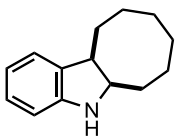
5,5a,6,7,8,9,10,10a-Octahydrocyclohepta[b]indole (S2t)



Following the **general procedure C** for 1 h, indole **S1t** (0.300 g, 1.62 mmol) afforded indoline **S2t** (0.280 g, 92%) as a white amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.[11]

R_f=0.68 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.01 – 6.93 (m, 2H), 6.68(t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 7.6 Hz, 1H), 4.07 – 4.01 (m, 1H), 3.47 (td, *J* = 10.4, 3.9 Hz, 1H), 2.00 – 1.93 (m, 1H), 1.89 – 1.69 (m, 6H), 1.44 – 1.32 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.3, 133.7, 127.5, 124.3, 118.3, 108.6, 63.6, 47.5, 33.7, 31.5, 30.0, 26.2.

5a,6,7,8,9,10,11,11a-Octahydro-5H-cycloocta[b]indole (S2u)

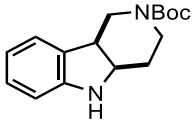


Following the **general procedure C** for 1 h, indole **S1u** (0.250 g, 1.25 mmol) afforded indoline **S2u** (0.221 g,

88%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.[13]

***R**f*=0.68 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.07 (d, *J* = 7.4 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.71 (t, *J* = 7.4 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 3.88 (t, *J* = 9.9 Hz, 1H), 3.21 (t, *J* = 9.7 Hz, 1H), 2.01 (dq, *J* = 45.0, 12.4, 11.5 Hz, 2H), 1.78 – 1.50 (m, 10H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 149.5, 135.4, 127.3, 124.3, 118.6, 108.6, 63.9, 46.2, 30.3, 30.1, 28.8, 27.7, 25.9, 25.5.

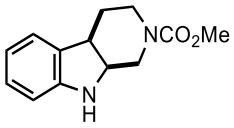
***tert*-Butyl 1,3,4,4a,5,9b-hexahydro-2H-pyrido[4,3-b]indole-2-carboxylate (S2v)**



Following the **general procedure C** for 2 h, indole **S1v** (0.200 g, 0.734 mmol) afforded indoline **S2v** (0.127 g, 63%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.12 (d, *J* = 7.1 Hz, 1H), 7.05 (td, *J* = 7.7, 1.3 Hz, 1H), 6.73 (td, *J* = 7.4, 1.0 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 3.97 (dt, *J* = 7.4, 5.0 Hz, 1H), 3.45 – 3.27 (m, 5H), 1.93 – 1.84 (m, 1H), 1.77 – 1.71 (m, 1H), 1.45 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 155.1, 151.0, 128.1, 124.4, 119.1, 110.1, 79.6, 57.6, 43.9, 41.2, 40.1, 39.5, 28.6, 28.2; **HRMS** calcd. for $C_{16}H_{23}N_2O_2^+$ $[M + H]^+$ 275.1754, found 275.1759.

Methyl 1,3,4,4a,9,9a-hexahydro-2H-pyrido[3,4-b]indole-2-carboxylate (S2w)

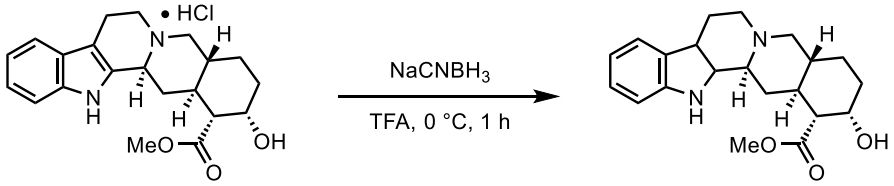


Following the **general procedure C** for 1 h, indole **S1w** (0.500 g, 1.84 mmol) afforded indoline **S2w** (0.262 g, 52%) as a white amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.07 – 7.01 (m, 2H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 3.97 – 3.86 (m, 2H), 3.68 (s, 3H), 3.58 – 3.53 (m, 1H), 3.39 – 3.34 (m, 3H),

2.04 – 1.96 (m, 1H), 1.87 – 1.79 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.6, 131.2, 127.9, 123.7, 119.0, 109.8, 57.4, 52.6, 44.4, 41.1, 39.3, 26.4 ; **HRMS** calcd. for $C_{13}H_{17}N_2O_2^+$ $[M + H]^+$ 233.1285, found 233.1288.

Methyl (1R,2S,4aR,13bS,14aS)-2-hydroxy-1,2,3,4,4a,5,7,8,8a,13,13a,13b,14,14a-tetradecahydroindolo [2',3':3,4]pyrido [1,2-b]isoquinoline-1-carboxylate (S2x)

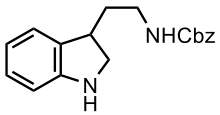


yohimbine hydrochloride **S2x**

To an oven-dried round-bottom flask equipped with a stir bar and septum were added yohimbine hydrochloride (0.100 g, 0.256 mmol, 1.0 equiv) and TFA (5 mL) at 23 °C. The resulting solution was cooled to 0 °C, and $NaBH_3CN$ (48.2 mg, 0.767 mmol, 3.0 equiv) was added to the solution. The reaction mixture was stirred for 1 h before it was directly concentrated under reduced pressure. The crude product was re-dissolved in CH_2Cl_2 (20 mL) and basified to pH 9−10 using $NH_3·H_2O$ (25.0−30.0 wt% in H_2O). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layer was washed with brine (1 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, CH_2Cl_2:MeOH = 1:0 → 9:1) to afford indoline **S2x** (83.0 mg, 91%) as a pale yellow viscous oil as a single diastereomer, which is consistent with the literature observations.[1]

***R**$_f$*=0.31 (silica gel, CH_2Cl_2:MeOH = 9:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.05 (d, *J* = 7.2 Hz, 1H), 6.97 (t, *J* = 7.7 Hz, 1H), 6.67 – 6.64 (m, 2H), 4.25 (s, 1H), 3.69 (s, 3H), 3.55 (d, *J* = 4.8 Hz, 1H), 2.99 (dt, *J* = 12.5, 6.6 Hz, 1H), 2.88 (d, *J* = 11.4 Hz, 1H), 2.83 (d, *J* = 11.8 Hz, 1H), 2.51 (d, *J* = 11.6 Hz, 1H), 2.35 – 2.27 (m, 2H), 2.13 (t, *J* = 10.3 Hz, 1H), 1.91 – 1.89 (m. 3H), 1.79 (dd, *J* = 14.1, 6.3 Hz, 1H), 1.65 (t, *J* = 12.6 Hz, 1H), 1.55 – 1.43 (m, 3H), 1.38 – 1.28 (m, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 175.0, 151.5, 135.6, 128.5, 124.1, 119.8, 111.5, 68.4, 64.2, 64.0, 62.4, 54.7, 53.7, 52.0, 49.8, 41.0, 40.6, 37.1, 35.0, 33.3, 30.1, 24.0; **HRMS** calcd. for $C_{21}H_{29}N_2O_3^+$ $[M + H]^+$ 357.2173, found 357.2180.

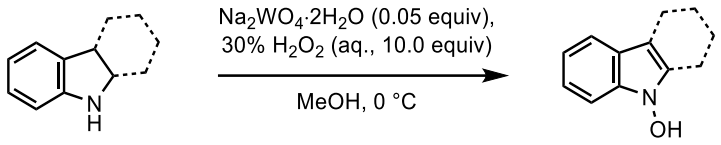
Benzyl (2-(indolin-3-yl)ethyl)carbamate (S2a')



Following the **general procedure B**, tryptamine **S1a'** (3.50 g, 16.0 mmol) afforded indoline **S2a'** (3.30 g, 94%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4). R_f=0.18 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (500 MHz, $CDCl_3$): 7.36 (d, J = 4.3 Hz, 4H), 7.34 – 7.28 (m, 1H), 7.10 (d, J = 7.3 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.74 (t, J = 7.5 Hz, 1H), 6.68 (d, J = 7.8 Hz, 1H), 5.10 (s, 2H), 4.89 (s, 1H), 3.71 (t, J = 8.7 Hz, 1H), 3.33 (q, J = 7.2 Hz, 1H), 3.27 (t, J = 7.4 Hz, 1H), 2.01 (dq, J = 13.2, 6.3 Hz, 1H), 1.77 (dt, J = 13.8, 7.0 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 156.5, 151.2, 136.6, 132.0, 128.4, 128.0, 127.6, 123.8, 118.6, 109.6, 66.5, 53.1, 39.4, 39.0, 34.3; **HRMS** calcd. for $C_{12}H_{17}N_2O_2^+$ $[M + H]^+$ 221.1285, found 221.1278.

2.3. Preparation of *N*-Hydroxyindole Derivatives

General procedure D



S2 **1**

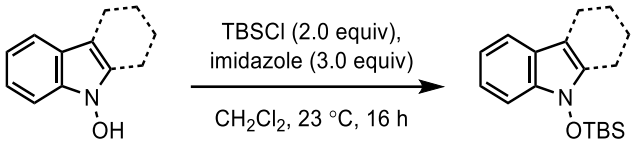
The compounds were synthesized according to a known literature procedure.[14] To an oven-dried round-bottom flask equipped with a stir bar and septum were added indoline **S2** (1.0 equiv) and MeOH (0.1 M in **S2**) at 23 °C. The resulting solution was cooled to 0 °C, and sodium tungstate dihydrate (0.05 equiv) and H_2O_2 (30 wt% in H_2O, 10.0 equiv) were successively added to the solution. The reaction mixture was stirred while the reaction was monitored by TLC. After completion of reaction, the reaction mixture was quenched with H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with H_2O three times, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford *N*-hydroxyindole **1**. The resulting crude product was used directly for the subsequent reaction without further purification.

note: In most cases, *N*-hydroxyindoles are unstable and slowly undergo decomposition, thus was unable to be stored for an extended period of time. However, most of *N*-hydroxyindoles could be obtained in excellent state which are clean enough to be characterized without purification. *N*-hydroxyindoles enlisted in this section were characterized without further purification (**1a–1o**, **1s**, **1x**) or otherwise protected with TBS group (**1p'**, **1q'**, **1r'**, **1v'**, **1w', 1a''**) for characterization. In case of the *N*-hydroxyindoles **1t** and **1u**, the products could be obtained in affordable quality. However, they could not be fully characterized due to their fast decomposition.

Determination of the reaction yield for the preparation of *N*-hydroxyindoles: The crude product was dissolved in CH_2Cl_2 to provide a solution with a total volume of 10.0 mL. 1.0 mL of the resulting solution was syringed out and dried separately in a 4 mL vial. To the 4 mL vial containing the separated sample was added 10.0 μL of 1,1,2,2-tetrachloroethane (TCE) as an internal standard and the resulting mixture was dissolved entirely in d4-methanol. The yield of product was determined by the integration of peaks from the ^{1}H NMR spectra relative to the internal standard, TCE. The calculated amount of the product in the sample (A) was then multiplied by 10 to

provide the total mass of the *N*-hydroxyindole product. The remaining 9.0 mL of the stock solution was dried under reduced pressure and used directly for the next step. The calculated amount of the product in the sample (A) was multiplied by 9 to provide the quantity of the starting material for the next reaction.

General Procedure E

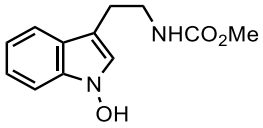


1 **1'**

For compounds **1p'**, **1q'**, **1r'**, **1v'**, **1w', 1a''**:

To an oven-dried round-bottom flask equipped with a stir bar and septum were added crude *N*-hydroxyindole **1** (1.0 equiv) and CH_2Cl_2 (0.2 M in **1**) at 23 °C, followed by TBSCl (2.0 equiv) and imidazole (3.0 equiv). The resulting mixture was stirred for 16 h before it was quenched with H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford TBS protected *N*-hydroxyindole.

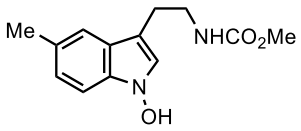
Methyl (2-(1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1a)



Following the **general procedure D** for 2 h, indoline **S2a** (0.120 g, 0.545 mmol) afforded *N*-hydroxyindole **1a** (93.0 mg, 73%) as a yellow oil and was used directly in the subsequent reaction without further purification.

***R**f*=0.45 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.53 (d, *J* = 8.1 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 7.10 (s, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 3.62 (s, 3H), 3.36 (t, *J* = 7.5 Hz, 2H), 2.89 (t, *J* = 7.7 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 135.7, 125.0, 124.4, 122.7, 119.7, 119.5, 109.2, 108.8, 75.8, 52.4, 42.8, 26.6; **HRMS** calcd. for $C_{12}H_{15}N_2O_3^+$ $[M + H]^+$ 235.1077, found 235.1077.

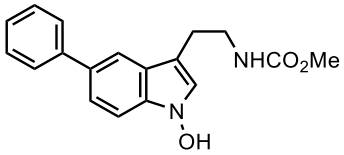
Methyl (2-(1-hydroxy-5-methyl-1H-indol-3-yl)ethyl)carbamate (1b)



Following the **general procedure D** for 2 h, indoline **S2b** (75.0 mg, 0.320 mmol) afforded *N*-hydroxyindole **1b**

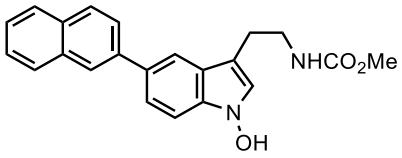
(48.0 mg, 60%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, MeOD): δ 7.32 (s, 1H), 7.23 (d, *J* = 8.3 Hz, 1H), 7.04 (s, 1H), 6.97 (dd, *J* = 8.4, 1.6 Hz, 1H), 3.62 (s, 3H), 3.34 (t, *J* = 7.4 Hz, 2H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.41 (s, 3H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 134.3, 128.8, 125.3, 124.5, 124.3, 119.1, 109.0, 108.2. 52.4, 42.8, 26.6, 21.6; **HRMS** calcd. for $C_{13}H_{17}N_2O_3^+$ $[M + H]^+$ 249.1234, found 249.1233.

Methyl (2-(1-hydroxy-5-phenyl-1H-indol-3-yl)ethyl)carbamate (1c)



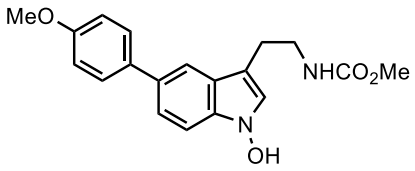
Following the **general procedure D** for 2 h, indoline **S2c** (60.0 mg, 0.202 mmol) afforded *N*-hydroxyindole **1c** (29.0 mg, 47%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.40 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.76 (s, 1H), 7.64 (d, *J* = 7.7 Hz, 2H), 7.44 – 7.37 (m, 4H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.14 (s, 1H), 3.60 (s, 3H), 3.39 (t, *J* = 7.3 Hz, 2H), 2.94 (t, *J* = 7.4 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 144.0, 135.1, 133.6, 129.6, 128.1, 127.2, 125.6, 125.1, 122.4, 118.0, 109.6, 109.4, 52.4, 43.0, 26.6; **HRMS** calcd. for $C_{18}H_{17}N_2O_3^-$ $[M - H]^-$ 309.1245, found 309.1241.

Methyl (2-(1-hydroxy-5-(naphthalen-2-yl)-1H-indol-3-yl)ethyl)carbamate (1d)



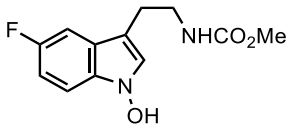
Following the **general procedure D** for 4 h, indoline **S2d** (75.0 mg, 0.216 mmol) afforded *N*-hydroxyindole **1d** (56.0 mg, 72%) as a brown oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, MeOD): δ 8.10 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 3H), 7.87 – 7.83 (m, 2H), 7.59 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.50 – 7.42 (m, 3H), 7.17 (s, 1H), 3.61 (s, 3H), 3.42 (t, *J* = 7.3 Hz, 2H), 2.97 (t, *J* = 7.3 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 159.7, 141.4, 135.4, 135.2, 133.7, 133.3, 129.2, 129.0, 128.6, 127.1, 127.1, 126.4, 126.1, 125.7, 125.2, 122.6, 118.4, 109.7, 109.5, 52.4, 43.1, 26.6; **HRMS** calcd. for $C_{22}H_{21}N_2O_3^+$ $[M + H]^+$ 361.1547, found 361.1545.

Methyl (2-(1-hydroxy-5-(4-methoxyphenyl)-1H-indol-3-yl)ethyl)carbamate (1e)



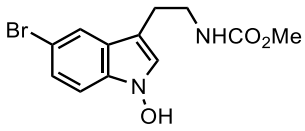
Following the **general procedure D** for 2 h, indoline **S2e** (75.0 mg, 0.230 mmol) afforded *N*-hydroxyindole **1e** (44.6 mg, 57%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.27 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.70 (s, 1H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.38 (s, 2H), 7.12 (s, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 3.81 (s, 3H), 3.60 (s, 3H), 3.38 (t, *J* = 7.3 Hz, 2H), 2.92 (t, *J* = 7.4 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 159.9, 159.6, 136.6, 134.9, 133.3, 129.1, 125.6, 125.0, 122.2, 117.4, 115.1, 109.5, 109.3, 55.7, 52.4, 43.0, 26.6; **HRMS** calcd. for $C_{19}H_{21}N_2O_4^+$ $[M + H]^+$ 341.1496, found 341.1504.

Methyl (2-(5-fluoro-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1f)



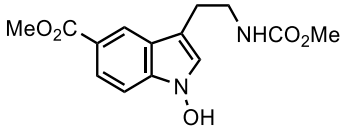
Following the **general procedure D** for 4 h, indoline **S2f** (50.0 mg, 0.210 mmol) afforded *N*-hydroxyindole **1f** (34.0 mg, 64%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.27 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.31 (dd, *J* = 8.9, 4.5 Hz, 1H), 7.22 (dd, *J* = 9.9, 2.4 Hz, 1H), 7.17 (s, 1H), 6.91 (td, *J* = 9.1, 2.4 Hz, 1H), 3.62 (s, 3H), 3.35 (t, *J* = 8.0 Hz, 2H), 2.85 (t, *J* = 7.4 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 158.9 (d, *J* = 232.4 Hz), 132.4, 126.1, 125.2 (d, *J* = 9.7 Hz), 110.9 (d, *J* = 26.7 Hz), 110.2 (d, *J* = 9.7 Hz), 108.7, 104.2 (d, *J* = 23.8 Hz), 52.4, 42.7, 26.5; **^{19}F NMR** (376 MHz, MeOD): δ –128.0 (td, *J* = 9.3, 4.2 Hz); **HRMS** calcd. for $C_{12}H_{12}FN_2O_3^-$ $[M - H]^-$ 251.0837, found 251.0832.

Methyl (2-(5-bromo-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1g)



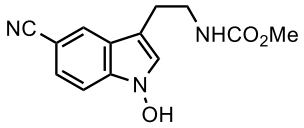
Following the **general procedure D** for 2.5 h, indoline **S2g** (0.100 g, 0.334 mmol) afforded *N*-hydroxyindole **1g** (57.0 mg, 54%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. R_f=0.41 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.68 (s, 1H), 7.26 (d, *J* = 8.7 Hz, 1H), 7.21 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.14 (s, 1H), 3.61 (s, 3H), 3.33 (t, *J* = 7.3 Hz, 2H), 2.84 (t, *J* = 7.3 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 134.1, 126.7, 125.7, 125.4, 122.1, 112.8, 110.9, 108.6, 52.4, 42.8, 26.3; **HRMS** calcd. for $C_{12}H_{12}BrN_2O_3^-$ [M − H]$^-$ 311.0037, found 311.0033.

Methyl 1-hydroxy-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indole-5-carboxylate (1h)



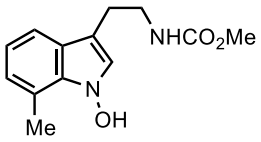
Following the **general procedure D** for 6 h, indoline **S2h** (70.0 mg, 0.252 mmol) afforded *N*-hydroxyindole **1h** (45.0 mg, 61%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. R_f=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, MeOD): δ 8.32 (s, 1H), 7.83 (dd, *J* = 8.7, 1.4 Hz, 1H), 7.39 (d, *J* = 8.7 Hz, 1H), 7.23 (s, 1H), 3.90 (s, 3H), 3.62 (s, 3H), 3.37 (t, *J* = 7.2 Hz, 2H), 2.94 (t, *J* = 7.2 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 170.0, 159.6, 137.4, 126.1, 124.5, 123.9, 122.9, 121.6, 110.9, 109.0, 52.4, 52.3, 42.8, 26.3; **HRMS** calcd. for $C_{14}H_{15}N_2O_5^-$ [M − H]$^-$ 291.0987, found 291.0985.

Methyl (2-(5-cyano-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1i)



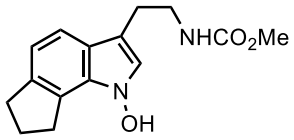
Following the **general procedure D** for 6 h, indoline **S2i** (25.3 mg, 0.103 mmol) afforded *N*-hydroxyindole **1i** (17.1 mg, 64%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. R_f=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, MeOD): δ 8.02 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 1H), 7.41 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.31 (s, 1H), 3.61 (s, 3H), 3.36 (t, *J* = 7.2 Hz, 3H), 2.92 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 136.4, 126.9, 125.8, 125.3, 124.8, 121.8, 110.5, 110.3, 102.2, 52.4, 42.7, 26.2 ; **HRMS** calcd. for $C_{13}H_{14}N_3O_3^+$ [M + H]$^+$ 260.1030, found 260.1024.

Methyl (2-(1-hydroxy-7-methyl-1H-indol-3-yl)ethyl)carbamate (1j)



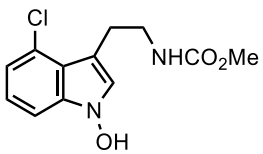
Following the **general procedure D** for 2 h, indoline **S2j** (80.0 mg, 0.341 mmol) afforded *N*-hydroxyindole **1j** (39.6 mg, 47%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, MeOD): δ 7.33 (d, *J* = 7.6 Hz, 1H), 7.03 (s, 1H), 6.90 – 6.80 (m, 2H), 3.62 (s, 3H), 3.35 (t, *J* = 7.5 Hz, 2H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.67 (s, 3H); **^{13}C NMR** (101 MHz, MeOD): δ 159.6, 134.3, 125.7, 125.3, 124.7, 121.7, 120.0, 117.2, 108.8, 52.4, 42.7, 26.6, 18.3; **HRMS** calcd. for $C_{13}H_{17}N_2O_3^+$ $[M + H]^+$ 249.1234, found 249.1234.

Methyl (2-(1-hydroxy-1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)ethyl)carbamate (1k)



Following the **general procedure D** for 2 h, indoline **S2k** (50.0 mg, 0.192 mmol) afforded *N*-hydroxyindole **1k** (40.5 mg, 77%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, MeOD): δ 7.29 (d, *J* = 8.1 Hz, 1H), 6.97 (s, 1H), 6.88 (d, *J* = 8.1 Hz, 1H), 3.61 (s, 3H), 3.35 – 3.27 (m, 4H), 2.94 (t, *J* = 7.4 Hz, 2H), 2.84 (t, *J* = 7.5 Hz, 2H), 2.14 (qui, *J* = 7.4 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 139.6, 132.9, 125.4, 124.1, 123.9, 117.6, 116.7, 109.2, 52.4, 42.7, 33.6, 31.4, 26.8, 26.5; **HRMS** calcd. for $C_{15}H_{19}N_2O_3^+$ $[M + H]^+$ 275.1390, found 275.1389.

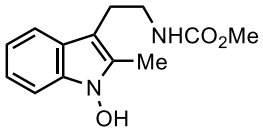
Methyl (2-(4-chloro-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1l)



Following the **general procedure D** for 5 h, indoline **S2l** (50.0 mg, 0.196 mmol) afforded *N*-hydroxyindole **1l** (37.1 mg, 70%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.

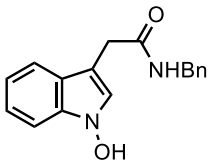
***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, MeOD): δ 7.30 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.17 (s, 1H), 7.05 (t, *J* = 7.9 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 3.61 (s, 3H), 3.40 (t, *J* = 7.3 Hz, 2H), 3.12 (t, *J* = 7.3 Hz, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 137.0, 127.1, 126.1, 123.1, 121.3, 120.6, 108.8, 108.3, 52.4, 43.8, 27.5; **HRMS** calcd. for $C_{12}H_{14}ClN_2O_3^+$ $[M + H]^+$ 269.0688, found 269.0685.

Methyl (2-(1-hydroxy-2-methyl-1H-indol-3-yl)ethyl)carbamate (1m)



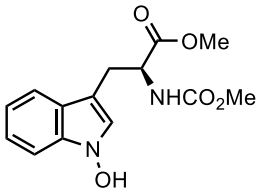
Following the **general procedure D** for 2 h, indoline **S2m** (33.6 mg, 0.143 mmol) afforded *N*-hydroxyindole **1m** (23.7 mg, 67%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.60 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.46 (d, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.96 (t, *J* = 7.4 Hz, 1H), 3.62 (s, 1H), 3.27 (t, *J* = 7.3 Hz, 2H), 2.87 (t, *J* = 7.2 Hz, 2H), 2.36 (s, 3H); **^{13}C NMR** (126 MHz, MeOD): δ 159.6, 135.3, 133.1, 124.9, 121.6, 119.7, 118.4, 108.6, 104.6, 52.3, 42.8, 25.8, 8.9; **HRMS** calcd. for $C_{13}H_{17}N_2O_3^+$ $[M + H]^+$ 249.1234, found 249.1233.

***N*-Benzyl-2-(1-hydroxy-1H-indol-3-yl)acetamide (1n)**



Following the **general procedure D** for 1.5 h, indoline **S2n** (40.8 mg, 0.153 mmol) afforded *N*-hydroxyindole **1n** (23.2 mg, 54%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.58 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.52 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.37 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.26 – 7.18 (m, 6H), 7.16 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.00 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 4.35 (s, 2H), 3.66 (s, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 174.6, 139.9, 135.6, 129.4, 128.5, 128.1, 125.6, 124.8, 122.9, 120.0, 119.7, 109.3, 104.8, 44.2, 33.7; **HRMS** calcd. for $C_{17}H_{17}N_2O_2^+$ $[M + H]^+$ 281.1285, found 281.1282.

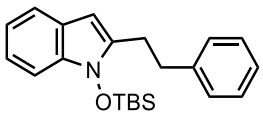
Methyl (S)-3-(1-hydroxy-1H-indol-3-yl)-2-((methoxycarbonyl)amino)propanoate (1o)



Following the **general procedure D** for 2 h, indoline **S2o** (70.0 mg, 0.252 mmol) afforded *N*-hydroxyindole **1o** (48.5 mg, 66%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.

***R**f*=0.44 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, MeOD): δ 7.50 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.17 – 7.12 (m, 2H), 7.01 (t, *J* = 7.5 Hz, 1H), 4.47 (t, *J* = 6.7 Hz, 1H) 3.64 (s, 3H), 3.59 (s, 3H), 3.25 (dd, *J* = 14.6, 5.7 Hz, 1H), 3.10 (dd, *J* = 14.6, 7.9 Hz, 1H); **^{13}C NMR** (101 MHz, MeOD): δ 174.3, 159.0, 135.4, 125.2, 124.9, 122.8, 119.9, 119.3, 109.3, 106.1, 56.5, 52.7, 28.4; **HRMS** calcd. for $C_{14}H_{17}N_2O_5^+$ $[M + H]^+$ 293.1132, found 293.1138.

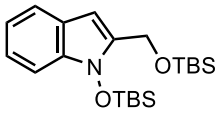
1-((*tert*-Butyldimethylsilyl)oxy)-2-phenethyl-1H-indole (1p')



Following the **general procedure D** for 1.5 h, indoline **S2p** (30.0 mg, 0.134 mmol) afforded *N*-hydroxyindole **1p** as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, crude *N*-hydroxyindole **1p** underwent TBS protection following the **general procedure E** to afford TBS-protected *N*-hydroxyindole **1p'** (27.4 mg, 0.0781 mmol, 58% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.30 (m, 3H), 7.26 – 7.21 (m, 3H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.16 (s, 1H), 3.06 (s, 4H), 1.14 (s, 9H), 0.27 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 141.5, 139.2, 134.8, 128.6, 128.5, 126.2, 124.1, 121.0, 120.0, 119.6, 109.0, 95.5, 34.6, 27.9, 26.1, 18.4, –3.7; **HRMS** calcd. for $C_{22}H_{30}NOSi^+$ $[M + H]^+$ 352.2091, found 352.2091.

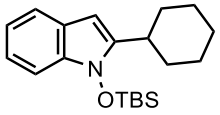
1-((*tert*-Butyldimethylsilyl)oxy)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)-1H-indole (1q')



Following the **general procedure D** for 1.5 h, indoline **S2q** (70.0 mg, 0.266 mmol) afforded *N*-hydroxyindole **1q** as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, crude *N*-hydroxyindole **1q** underwent TBS protection following the **general procedure E** to afford TBS-protected *N*-hydroxyindole **1q'** (71.9 mg, 0.190mmol, 72% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

R_f=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.33 (s, 1H), 4.84 (s, 2H), 1.14 (s, 9H), 0.95 (s, 9H), 0.29 (s, 6H), 0.11 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 138.9, 135.3, 124.1, 121.5, 120.6, 119.8, 109.2, 96.9, 57.3, 26.1, 18.5, 18.5, –4.0, –5.1; **HRMS** calcd. for $C_{21}H_{38}NO_2Si_2^+$ $[M + H]^+$ 392.2436, found 392.2435.

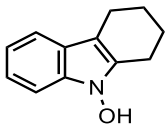
1-((*tert*-Butyldimethylsilyl)oxy)-2-cyclohexyl-1H-indole (1r')



Following the **general procedure D** for 1.5 h, indoline **S2r** (20.0 mg, 0.0993 mmol) afforded *N*-hydroxyindole **1r** as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, crude *N*-hydroxyindole **1r** underwent TBS protection following the **general procedure E** to afford TBS-protected *N*-hydroxyindole **1r'** (18.4 g, 0.0558 mmol, 56% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

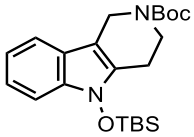
R_f=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.10 (td, *J* = 7.1, 0.9 Hz, 1H), 7.02 (td, *J* = 7.5, 0.8 Hz, 1H), 6.08 (s, 1H), 2.81 – 2.75 (m, 1H), 2.08 (d, *J* = 8.4 Hz, 2H), 1.86 – 1.84 (m, 2H), 1.76 (d, *J* = 11.7 Hz, 1H), 1.42 – 1.24 (m, 6H), 1.14 (s, 9H), 0.24 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 145.0, 134.1, 124.0, 120.6, 120.0, 119.3, 108.9, 92.8, 35.1, 32.8, 26.7, 26.3, 26.1, 18.4, –3.8; **HRMS** calcd. for $C_{20}H_{32}NOSi^+$ $[M + H]^+$ 330.2248, found 330.2246.

1,2,3,4-Tetrahydro-9H-carbazol-9-ol (1s)



Following the **general procedure D** for 1.5 h, indoline **S2s** (30.0 mg, 0.173 mmol) afforded *N*-hydroxyindole **1s** (25.0 mg, 77%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. ***R**f*=0.65 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (400 MHz, MeOD): δ 7.30 (dd, *J* = 14.5, 7.9 Hz, 2H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.92 (t, *J* = 7.4 Hz, 1H), 2.69 (dt, *J* = 36.8, 4.8 Hz, 4H), 1.91 – 1.82 (m, 4H); **^{13}C NMR** (101 MHz, MeOD): δ 135.9, 135.15 124.6, 121.5, 119.4, 118.3, 108.6, 105.9, 24.5, 24.0, 21.9, 21.8; **HRMS** calcd. for $C_{12}H_{14}NO^+$ $[M + H]^+$ 188.1070, found 188.1067.

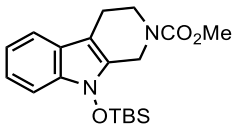
***tert*-Butyl 5-((*tert*-butyldimethylsilyl)oxy)-1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate (1v')**



Following the **general procedure D** for 2 h, indoline **S2v** (50.0 mg, 0.182 mmol) afforded *N*-hydroxyindole **1v** as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, *N*-hydroxyindole **1v** underwent TBS protection following the **general procedure E** to afford TBS-protected *N*-hydroxyindole **1v'** (55.6 mg, 0.138 mmol, 76% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 4.61 (br s, 2H), 3.78 (br s, 2H), 2.79 (br s, 2H), 1.51 (s, 9H), 1.11 (s, 9H), 0.29 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 136.6, 121.7, 119.9, 117.7, 109.5, 80.1, 41.4, 40.6, 28.7, 26.0, 22.7, 18.3, –4.0; **HRMS** calcd. for $C_{22}H_{35}N_2O_3Si^+$ $[M + H]^+$ 403.2412, found 403.2412.

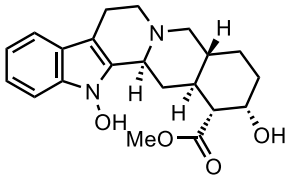
Methyl 9-((*tert*-butyldimethylsilyl)oxy)-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate (1w')



Following the **general procedure D** for 2 h, indoline **S2w** (50.0 mg, 0.215 mmol) afforded *N*-hydroxyindole **1w** as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, *N*-hydroxyindole **1w** underwent TBS protection following the **general procedure E** to afford TBS-protected *N*-hydroxyindole **1w'** (55.8 mg, 0.155 mmol, 72% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 4.64 (d, *J* = 19.6 Hz, 2H), 3.83 – 3.76 (m, 2H), 3.77 (s, 3H), 2.79 (t, *J* = 5.8 Hz, 2H), 1.12 (s, 9H), 0.32 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 156.5, 136.9, 132.3, 123.8, 122.0, 120.0, 118.2, 109.6, 106.3, 105.7, 53.0, 42.2, 41.4, 26.0, 21.5, 21.0, 18.3, –3.9; **HRMS** calcd. for $C_{19}H_{29}N_2O_3Si^+$ $[M + H]^+$ 361.1942, found 361.1941.

Methyl (1R,2S,4aR,13bS,14aS)-2,13-dihydroxy-1,2,3,4,4a,5,7,8,13,13b,14,14a-dodecahydroindolo [2',3':3,4]pyrido[1,2-b]isoquinoline-1-carboxylate (1x)

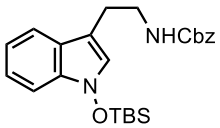


Following the **general procedure D** for 30 min, indoline **S2x** (40.0 mg, 0.112 mmol) afforded *N*-hydroxyindole **1x** (29.9 mg, 72%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. Analytic data is in agreement with the reported literature values.[1]

***R**f*=0.39 (silica gel, CH_2Cl_2:MeOH = 9:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.37 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 4.23 (q, *J* = 2.9 Hz, 1H), 3.74 (s, 3H), 3.64 (d, *J* = 11.7 Hz, 1H), 3.17 – 3.10 (m, 1H), 2.98 – 2.91 (m, 3H), 2.76 – 2.65 (m, 2H), 2.41 (t, *J* = 11.2 Hz, 1H), 2.33 (dd, *J* = 11.7, 2.6 Hz, 1H), 2.00 (qd, *J* = 11.5, 3.1 Hz, 1H), 1.92 (dq, *J* = 14.3, 3.3 Hz, 1H), 1.71 – 1.63 (m, 1H), 1.60 – 1.44 (m, 2H), 1.41 – 1.34 (m, 1H), 1.21 (q, *J* = 11.8 Hz, 1H); **^{13}C NMR** (126 MHz, MeOD): δ 175.4, 137.3,

134.8, 123.8, 122.4, 120.2, 118.7, 109.3, 105.1, 68.6, 62.3, 60.9, 54.0, 52.7, 52.0, 40.3, 37.6, 33.6, 33.5, 24.4, 22.5; **HRMS** calcd. for $C_{19}H_{29}N_2O_3Si^+$ $[M + H]^+$ 361.1942, found 361.1941.

Benzyl (2-(1-((*tert*-butyldimethylsilyl)oxy)-1H-indol-3-yl)ethyl)carbamate (1a'')



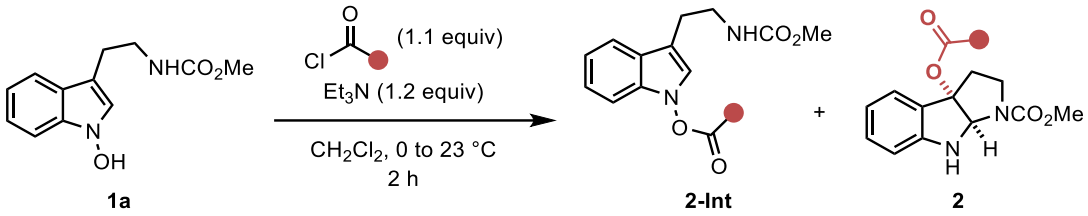
Following the **general procedure D** for 2 h, indoline **S2a'** (70.0 mg, 0.236 mmol) afforded *N*-hydroxyindole **1a'** as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, *N*-hydroxyindole **1a'** underwent TBS protection following the **general procedure E** to afford TBS-protected *N*-hydroxyindole **1a''** (66.2 mg, 0.156 mmol, 66% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

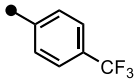
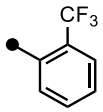
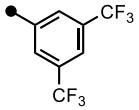
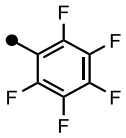
R_f=0.63 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, MeOD): δ 7.56 (d, *J* = 8.0 Hz, 1H), 7.35 – 7.26 (m, 5H), 7.26 (d, *J* = 8.2 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.07 (s, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 5.06 (s, 2H), 3.39 (t, *J* = 7.1 Hz, 2H), 2.91 (t, *J* = 7.1 Hz, 2H), 1.10 (s, 9H), 0.22 (s, 6H); **^{13}C NMR** (126 MHz, MeOD): δ 158.9, 138.5, 136.0, 129.5, 128.9, 128.7, 125.1, 124.9, 123.1, 122.6, 120.2, 119.8, 110.0, 109.8, 67.3, 42.7, 26.4, 26.2, 18.8, –4.7; **HRMS** calcd. for $C_{24}H_{33}N_2O_3Si^+$ $[M + H]^+$ 425.2255, found 425.2269.

3. Mechanistic Investigations

3.1. Identification of 2'-Substituent Effect in the Facilitated IHT Reaction (Scheme 1)

Table S1. Evaluation of 2'-substituents.[a]

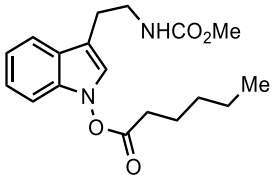


entry	2'-substituent ( )	yield of 2-Int (%)	yield of 2 (%)
1		62%	0%
2		65%	0%
3		60%[b]	5%[b]
4		30%[b]	30%[b]
5		9%[b]	39%[b]
6		0%	53%

[a]Reactions performed with benzoyl chloride (1.1 equiv) and Et_3N (1.2 equiv) in CH_2Cl_2 (0.05 M) at 0 to 23 °C for 2 h on 0.201 mmol scale. [b]**2-Int** and **2** were co-eluted from silica gel chromatography. The ratio between **2-Int** and **2** were determined by ^1H NMR analysis of the mix ture.

For characterization, the mixture obtained in entries 3, 4 and 5 was converted to pyrroloindoline **2** under separately performed thermal conditions since indolyl *N*-benzoate **2-Int** and pyrroloindoline **2** co-eluted under the various solvent systems.

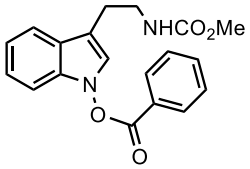
Methyl 3a-(hexanoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2a-Int)



Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to indolyl *N*-carboxylate **2a-Int** (41.1 mg, 62%) as a pale yellow oil.

***R**f*=0.60 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.9 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.19 – 7.13 (m, 2H), 6.98 (br s, 1H), 4.83 (s, 1H), 3.66 (s, 3H), 3.51 (q, *J* = 6.7 Hz, 2H), 2.94 (t, *J* = 6.8 Hz, 2H), 2.63 (t, *J* = 7.5 Hz, 2H), 1.82 (p, *J* = 7.4 Hz, 2H), 1.50 – 1.35 (m, 4H), 0.95 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 171.8, 157.2, 135.4, 124.7, 123.9, 123.5, 120.8, 119.3, 111.5, 108.9, 52.2, 41.1, 31.7, 31.3, 25.8, 24.7, 22.4; **HRMS** calcd. for $C_{18}H_{25}N_2O_4^+$ $[M + H]^+$ 333.1809, found 333.1810.

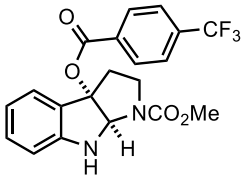
3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (2b-Int)



Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to indolyl *N*-carboxylate **2b-Int** (44.2 mg, 65%) as a pale yellow oil.

***R**f*=0.31 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.22 (d, *J* = 7.2 Hz, 2H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 3.5 Hz, 2H), 7.18 (ddd, *J* = 8.1, 4.6, 3.5 Hz, 1H), 7.10 (s, 1H), 4.83 (s, 1H), 3.67 (s, 3H), 3.55 (q, *J* = 6.6 Hz, 2H), 2.98 (t, *J* = 6.8 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 164.9, 157.2, 135.9, 134.7, 130.4, 129.1, 126.6, 125.0, 124.2, 123.7, 121.1, 119.4, 112.0, 109.2, 52.2, 41.1, 25.9; **HRMS** calcd. for $C_{19}H_{19}N_2O_4^+$ $[M + H]^+$ 339.1339, found 339.1338.

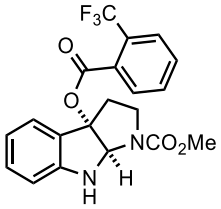
Methyl 3a-((4-(trifluoromethyl)benzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2c)



Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to an inseparable mixture of indolyl *N*-carboxylate **2c-Int** and pyrroloindoline **2c** (53.1 mg, 12:1, overall 65%) as a pale yellow oil. For characterization, the pure sample of **2c** was obtained as a sole product by the reaction of **1a** at 90 °C (**general procedure H**, Section 3.3).

R_f=0.63 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.10 (d, *J* = 8.1 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.61 and 7.55 (d, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 6.81 (q, *J* = 6.9 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 5.77 (s, 1H), 3.94 and 3.82 (t, *J* = 9.6 Hz, 1H), 3.80 and 3.73 (s, 3H), 3.26 – 3.20 (m, 1H), 3.09 and 2.99 (dd, *J* = 12.6, 5.9 Hz, 1H), 2.71 (q, *J* = 11.2 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 164.3, 155.7, 154.9, 151.1, 150.9, 134.8 (q, *J* = 32.5 Hz), 133.5, 131.4, 130.3, 126.7, 126.2, 125.5 (q, *J* = 4.2 Hz), 123.5 (q, *J* = 272.7 Hz), 119.8, 119.6, 110.6, 110.4, 95.1, 93.8, 80.4, 79.6, 53.0, 52.7, 45.6, 35.8, 35.7; **^{19}F NMR** (471 MHz, $CDCl_3$): δ −63.2; **HRMS** calcd. for $C_{20}H_{18}F_3N_2O_4^+$ $[M + H]^+$ 407.1213, found 407.1206.

Methyl 3a-((2-(trifluoromethyl)benzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2d)

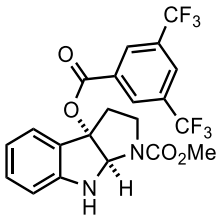


Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to an inseparable mixture of indolyl *N*-carboxylate **2d-Int** and pyrroloindoline **2d** (49.0 mg, 1:1, overall 60%) as a pale yellow oil. For characterization, the pure sample of **2d** was obtained as a sole product by the reaction of **1a** at 90 °C (**general procedure H**, Section 3.3).

R_f=0.50 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.74 – 7.68 (m, 2H), 7.62 and 7.58 (d, *J* = 7.5 Hz, 1H), 7.60 – 7.54 (m, 2H), 7.21 (t, *J* = 7.8 Hz, 1H), 6.82 (q, *J* = 7.2 Hz, 1H),

6.68 (d, *J* = 7.9 Hz, 1H), 5.71 and 5.70 (s, 1H), 3.92 and 3.81 (t, *J* = 9.8 Hz, 1H), 3.80 and 3.73 (s, 3H), 3.25 – 3.19 (m, 1H), 3.05 and 2.96 (dd, *J* = 12.9, 6.3 Hz, 1H), 2.78 – 2.69 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.6, 155.7, 154.9, 151.1, 150.8, 131.9, 131.5, 131.3, 131.2, 130.7, 128.7 (q, *J* = 32.6 Hz), 126.8 (q, *J* = 5.6 Hz), 126.6, 126.2, 125.5, 125.4, 123.5 (q, *J* = 272.7 Hz), 119.8, 119.5, 110.5, 110.4, 95.5, 94.3, 80.0, 79.3, 53.0, 52.7, 45.6, 35.2, 35.1; **^{19}F NMR** (471 MHz, $CDCl_3$): δ –58.9; **HRMS** calcd. for $C_{20}H_{18}F_3N_2O_4^+$ $[M + H]^+$ 407.1213, found 407.1204.

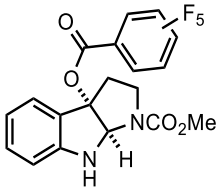
Methyl 3a-((3,5-bis(trifluoromethyl)benzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2e)



Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to an inseparable mixture of indolyl *N*-carboxylate **2e-Int** and pyrroloindoline **2e** (45.8 mg, 1:4, overall 48%) as a pale yellow oil. For characterization, the pure sample of **2e** was obtained as a sole product by the reaction of **1a** at 90 °C (**general procedure H**, Section 3.3).

***R*$_f$**=0.70 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.54 and 8.42 (s, 2H), 8.11 and 8.05 (s, 1H), 7.60 (dd, *J* = 20.2, 7.6 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 6.82 (q, *J* = 7.0 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 5.80 and 5.77 (s, 1H), 5.78 (d, *J* = 13.8 Hz, 1H), 3.96 and 3.86 (t, *J* = 9.5 Hz, 1H), 3.82 and 3.74 (s, 3H), 3.24 (tt, *J* = 11.5, 6.0 Hz, 1H), 3.13 and 3.07 (dd, *J* = 12.7, 6.2 Hz, 1H), 2.77 – 2.65 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 162.8, 155.7, 154.8, 151.2, 151.0, 132.7, 132.4, 132.35 (q, *J* = 26.0 Hz), 131.7, 130.4, 130.0, 127.0, 126.8, 126.7, 126.4, 125.0, 125.0, 122.93 (q, *J* = 272.9 Hz), 120.0, 119.7, 110.6, 110.5, 95.8, 94.6, 80.4, 79.7, 53.1, 52.8, 45.7, 35.7; **^{19}F NMR** (471 MHz, $CDCl_3$): δ –63.0, –63.0; **HRMS** calcd. for $C_{21}H_{17}F_6N_2O_4^+$ $[M + H]^+$ 475.1087, found 475.1077.

Methyl 3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2f)

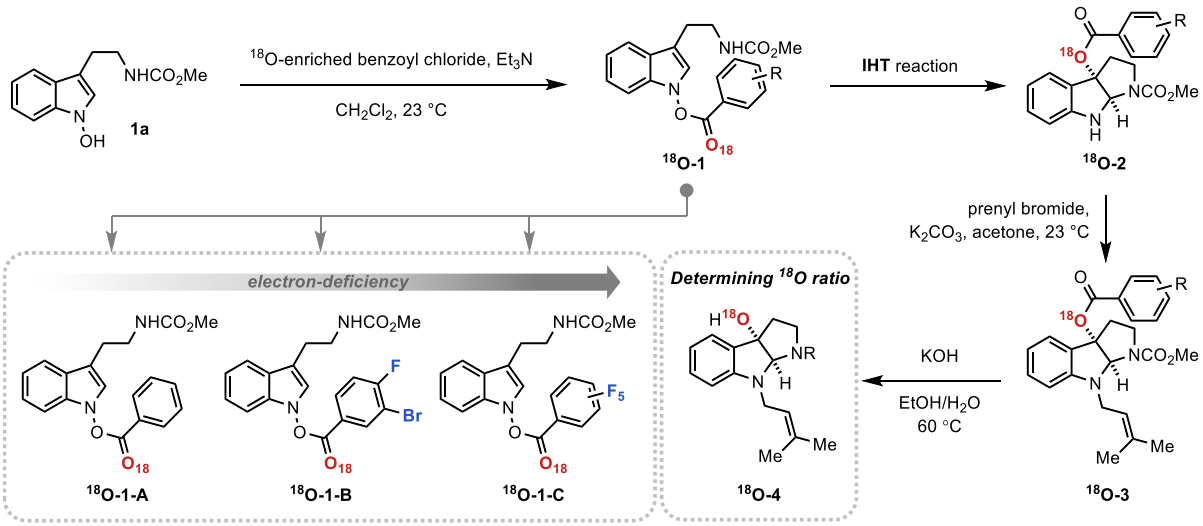


Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to pyrroloindoline **2f** (45.6 mg, 53%) as a pale yellow oil.

***R*$_f$**=0.56 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.56 and 7.53 (d, *J* = 8.7 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 6.83 (q, *J* = 7.2, 6.7 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.71 (d, *J* = 3.3 Hz, 1H), 3.92 and 3.82 (t, *J* = 9.7 Hz, 1H), 3.80 and 3.73 (s, 3H), 3.25 – 3.16 (m, 1H), 3.03 and 2.96 (dd, *J* = 12.6, 6.2 Hz, 1H), 2.70 (q, *J* = 10.7 Hz, 1H) ; **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.8, 155.6, 154.8, 151.2, 151.0, 147.2 – 144.0 (dm, *J* = 262.7 Hz), 145.1 – 141.9 (dm, *J* = 260.2 Hz), 139.5 – 136.1 (dm, *J* = 257.6 Hz), 131.7, 126.4, 126.1, 124.8, 124.7, 122.6, 120.5, 120.0, 119.7, 110.7, 110.5, 108.2 (t, *J* = 15.7 Hz), 96.6, 95.4, 80.1, 79.4, 53.0, 52.8, 45.5, 35.7, 35.6; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −139.6 (dp, *J* = 17.0, 5.8 Hz), −149.6 (dtt, *J* = 57.4, 20.7, 4.8 Hz), −161.8 – −162.0 (m); **HRMS** calcd. for $C_{19}H_{14}F_5N_2O_4^+$ $[M + H]^+$ 429.0868, found 429.0873.

3.2. ^{18}O Isotope Experiment (Figure 3)

Scheme S2. Overview of the ^{18}O labeling experiment.



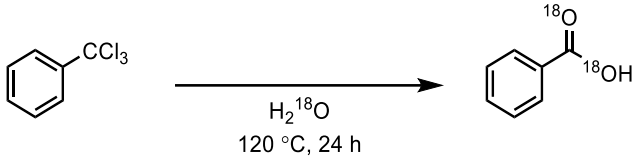
The general method for measuring ^{18}O saturation is as follows: First,^{18}O enriched acyl chlorides were prepared according to the literature procedures.[15] Indolyl *N*-carboxylates, **^{18}O-1-A** and **^{18}O-1-B**, were synthesized using the prepared ^{18}O-enriched acyl chlorides. These precursors were subsequently subjected to **IHT** reaction conditions to provide **^{18}O-2-A** and **^{18}O-2-B** respectively. In the case of **^{18}O-1-C**, upon acylation, the intermediate immediately underwent the desired **IHT** reaction to provide **^{18}O-2-C**. Independent HRMS analyses of acylation products of methanol with acyl chlorides used for the preparation of **^{18}O-1-A** and **^{18}O-1-B** had shown that the level of ^{18}O enrichment in the acyl chloride is directly reflected the acylation products. Also, it was shown that the level of ^{18}O enrichment for **^{18}O-1-A** and **^{18}O-1-B** remained unchanged after IHT reaction to provide **^{18}O-2-A** and **^{18}O-2-B** respectively. Therefore, the level of ^{18}O enrichment for **^{18}O-1-C** was estimated to be identical to that of **^{18}O-2-C**.

Detailed synthetic schemes for preparation of compounds are presented below.

3.2.1. Preparation of ^{18}O Labeled Compounds

3.2.1.1. Benzoyl substituent

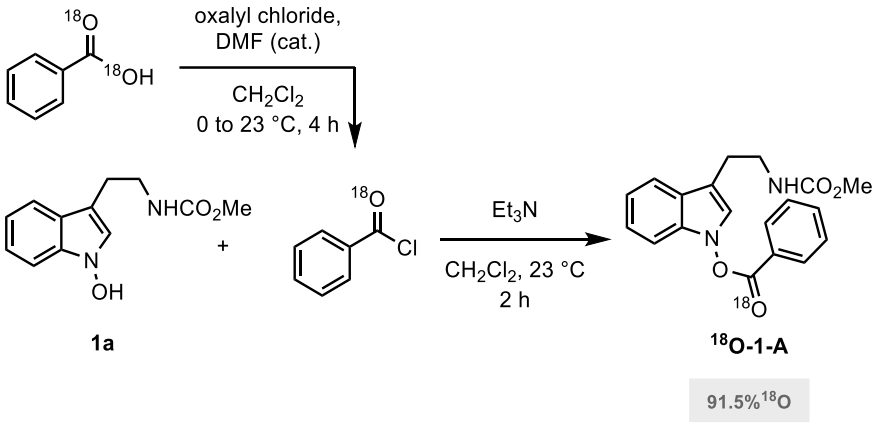
^{18}O-Benzoic acid



To an oven-dried heavy-wall pressure tube equipped with a stir bar and rubber septum were added α,α,α-trichlorotoluene (1.40 mL, 10.0 mmol, 1.0 equiv) and $H_2{}^{18}O$ (1.00 mL, 50.0 mmol, 5.0 equiv) at 23 °C. The rubber septum was replaced with a Teflon screw cap under N_2 and the resulting mixture was heated to 120 °C in a pre-heated oil bath and stirred for 24 h. After the reaction mixture was cooled to 23 °C, the white solid was formed and precipitate was collected by filtration. The resulting filter cake was washed with H_2O (1 × 3 mL), and the solid was dried *in vacuo*, to afford ^{18}O-benzoic acid (1.16 g, 92%) as a white solid. The resulting residue was used directly in the subsequent reaction without further purification. Analytic data is in agreement with the reported literature values.[16]

***R*$_f$**=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 8.3, 1.5 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 172.3, 134.0, 130.4, 129.5, 128.7; **HRMS** calcd. for $C_7H_5{}^{18}O_2^-$ $[M - H]^-$ 125.0380, found 125.0380; **Isotopic Incorporation:** [M+4] 96.8%, [M+2] 3.1%, [M+0] 0.1%.

3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (^{18}O-1-A)

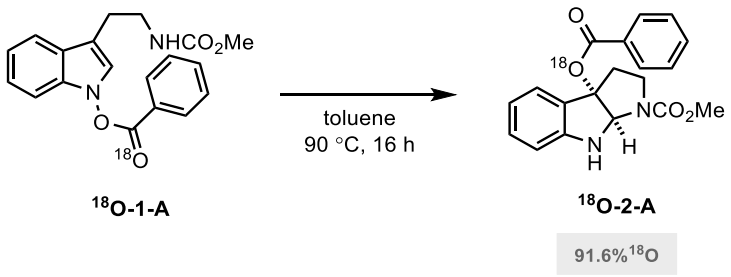


To an oven-dried two-neck round-bottom flask equipped with a stir bar, septum, and condenser were added ^{18}O-benzoic acid (126 mg, 1.00 mmol, 1.02 equiv), DMF (a few drops) and CH_2Cl_2 (3 mL) at 23 °C. The resulting solution was cooled to 0 °C and oxalyl chloride (126 μL, 1.47 mmol, 1.5 equiv) was added dropwise. The reaction mixture was stirred for 4 h at 23 °C, before it was directly concentrated under reduced pressure. The resulting ^{18}O-benzoyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1a** (0.230 g, 0.982 mmol, 1.0 equiv) and CH_2Cl_2 (10 mL) at 23 °C, followed by the crude benzoyl chloride and Et_3N (0.178 mL, 1.28 mmol, 1.3 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H_2O (10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was washed with brine (1 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (237 mg, 71%) as a pale yellow oil. The spectral data matched to those of compound **2b-Int** (See section 3.1).

***R**$_f$*=0.65 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.22 (d, *J* = 6.9 Hz, 2H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 2H), 7.27 – 7.25 (m, 2H), 7.18 (ddd, *J* = 8.1, 4.7, 3.5 Hz, 1H), 7.10 (s, 1H), 4.83 (s, 1H), 3.67 (s, 3H), 3.55 (q, *J* = 6.6 Hz, 2H), 2.98 (t, *J* = 6.9 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 164.9, 157.2, 135.9, 134.7, 130.4, 129.1, 126.6, 125.0, 124.2, 123.7, 121.1, 119.4, 112.0, 109.2, 52.2, 41.1, 25.9; **HRMS** calcd. for $C_{19}H_{18}N_2O_3{}^{18}ONa^+$ $[M + Na]^+$ 363.1201, found 363.1192; **Isotopic Incorporation:** [M+2] 91.5%, [M+0] 8.5%.

Methyl 3a-(benzoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-A)



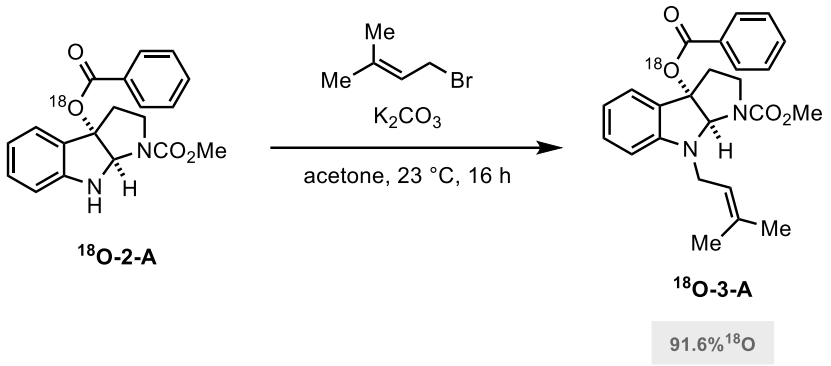
^{18}O-1-A **^{18}O-2-A**

91.6%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-1-A** (155 mg, 0.455 mmol, 1.0 equiv) and toluene (9 mL) at 23 °C. The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (98.3 mg, 63%) as a pale yellow oil.

***R**$_f$*=0.65 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 55:45 mixture of rotamers): δ 7.99 (d, *J* = 7.7 Hz, 2H), 7.63 and 7.42 (d, *J* = 7.6 Hz, 1H), 7.54 (br t, *J* = 8.3 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.80 (q, *J* = 6.9 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 5.78 (s, 1H), 3.93 and 3.80 (t, *J* = 9.7 Hz, 1H), 3.80 and 3.73 (s, 3H), 3.27 – 3.20 (m, 1H), 3.07 and 2.96 (dd, *J* = 12.9, 6.3 Hz, 1H), 2.78 – 2.64 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.3, 155.6, 154.8, 151.0, 150.7, 133.2, 131.0, 130.2, 129.8, 129.1, 128.4, 126.5, 126.3, 126.0, 119.6, 119.3, 110.3, 110.2, 94.5, 93.3, 80.4, 79.6, 52.8, 52.5, 45.5, 35.9, 35.8; **HRMS** calcd. for $C_{19}H_{19}N_2O_3{}^{18}O^+$ $[M + H]^+$ 341.1382, found 341.1373; **Isotopic Incorporation:** [M+2] 91.6%, [M+0] 8.4%.

Methyl 3a-(benzoyloxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-A)



^{18}O-2-A

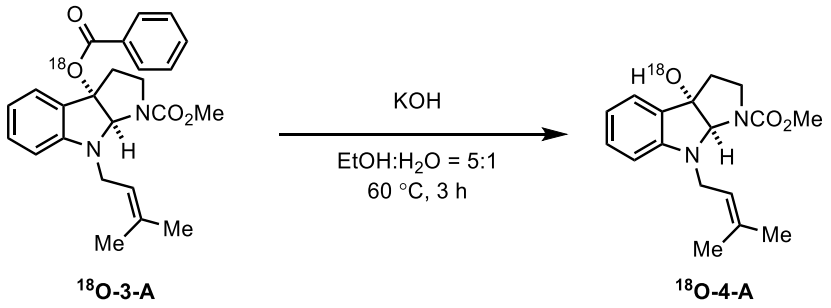
^{18}O-3-A

91.6%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-2-A** (98.3 mg, 0.289 mmol, 1.0 equiv) and acetone (7 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (50 μL, 0.434 mmol, 1.5 equiv) and K_2CO_3 (0.120 g, 0.867 mmol, 3.0 equiv). The resulting mixture was stirred for 16 h, before it was directly concentrated under reduced pressure and re-dissolved in CH_2Cl_2 (10 mL) and H_2O (10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (99.0 mg, 84%) as a pale yellow oil.

***R**$_f$*=0.38 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$, 50:50 mixture of rotamers): δ 7.98 (d, *J* = 7.7 Hz, 2H), 7.54 (br t, *J* = 7.3 Hz, 1H), 7.53 and 7.46 (d, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.7 Hz, 2H), 6.71 (t, *J* = 7.5 Hz, 2H), 6.53 (t, *J* = 8.5 Hz, 1H), 5.89 and 5.83 (s, 1H), 5.24 (s, 1H), 4.28 and 4.10 (dd, *J* = 16.3, 7.5 Hz, 1H), 4.07 (br t, *J* = 11.9, 10.4 Hz, 1H), 4.07 and 3.93 (br t, *J* = 9.8 Hz, 1H), 3.78 and 3.75 (s, 3H), 3.23 – 3.10 (m, 1H), 2.93 – 2.79 (m, 1H), 2.68 (t, *J* = 10.9 Hz, 1H), 1.78 (d, *J* = 14.6 Hz, 3H), 1.71 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): 165.2, 155.9, 155.1, 152.1, 134.8, 134.4, 133.2, 131.1, 130.4, 129.8, 128.4, 127.0, 126.8, 126.0, 125.5, 121.3, 121.0, 118.2, 108.5, 108.0, 94.6, 93.7, 85.0, 84.4, 52.8, 45.6, 45.5, 45.3, 45.0, 37.6, 25.9, 18.3, 18.2; **HRMS** calcd. for $C_{24}H_{27}N_2O_3{}^{18}O^+$ $[M + H]^+$ 409.2008, found 409.2003; **Isotopic Incorporation:** [M+2] 91.6%, [M+0] 8.4%.

Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-A)



^{18}O-3-A **^{18}O-4-A**

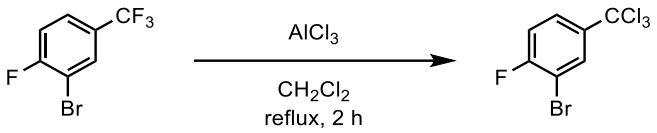
80.0%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-3-A** (99.0 mg, 0.242 mmol, 1.0 equiv) and EtOH: H_2O (5:1, 6 mL) at 23 °C, followed by KOH (20.4 mg, 0.363 mmol, 1.5 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and re-dissolved with CH_2Cl_2 (10 mL) and H_2O (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (57.2 mg, 78%) as a pale yellow oil.

***R**$_f$*=0.45 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 50:50 mixture of rotamers): δ 7.25 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.49 (s, 1H), 5.38 and 5.30 (s, 1H), 5.16 (s, 1H), 4.22 – 4.08 and 4.07 – 3.93 (m, 1H), 3.96 (br s, 1H), 3.96 and 3.83 (br s, 1H), 3.73 (s, 3H), 3.23 – 3.04 (m, 2H), 2.41 – 2.23 (m, 2H), 1.75 (d, *J* = 11.7 Hz, 3H), 1.69 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.4, 135.2, 130.8, 130.7, 130.5, 123.4, 123.2, 120.4, 120.3, 118.2, 108.4, 108.0, 87.7, 87.5, 86.9, 52.7, 45.8, 44.9, 44.4, 38.4, 25.9, 18.3; **HRMS** calcd. for $C_{17}H_{23}N_2O_2{}^{18}O^+$ $[M + H]^+$ 305.1746, found 305.1740; **Isotopic Incorporation:** [M+2] 80.0%, [M+0] 20.0%.

3.2.1.2. 3-Bromo-4-fluorobenzoyl substituent

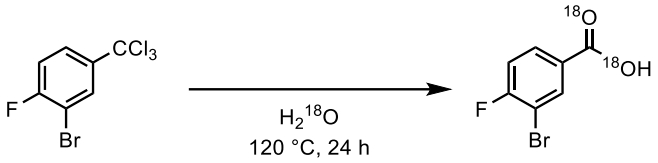
2-Bromo-1-fluoro-4-(trichloromethyl)benzene



To an oven-dried round-bottom flask equipped with a stir bar, septum, and condenser were added $AlCl_3$ (1.73 g, 13.0 mmol, 1.3 equiv) and CH_2Cl_2 (30 mL) at 23 °C. To a stirred mixture was added 3-bromo-4-fluorobenzotrifluoride (1.42 mL, 10.0 mmol, 1.0 equiv) dropwise via syringe. The reaction mixture was then heated to reflux in a pre-heated oil bath and stirred for 2 h, before it was cooled to 23 °C and quenched with iced water (15 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1) to afford 3-bromo-4-fluorobenzotrichloride (1.75 g, 60%) as a pale yellow liquid. Analytic data is in agreement with the reported literature values.

***R**f*=0.75 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.15 (dd, *J* = 6.2, 2.7 Hz, 1H), 7.87 (ddd, *J* = 9.1, 4.4, 2.5 Hz, 1H), 7.17 (ddd, *J* = 9.5, 7.8, 1.9 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 160.0 (d, *J* = 253.1 Hz), 141.6 (d, *J* = 3.8 Hz), 131.4, 126.8 (d, *J* = 8.1 Hz), 116. 3 (d, *J* = 23.3 Hz), 109.1 (d, *J* = 22.0 Hz), 95.6; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −103.7 – −104.3 (m); **HRMS** calcd. for $C_7H_4BrCl_3F^+$ $[M + H]^+$ 290.8541, found 290.8541.

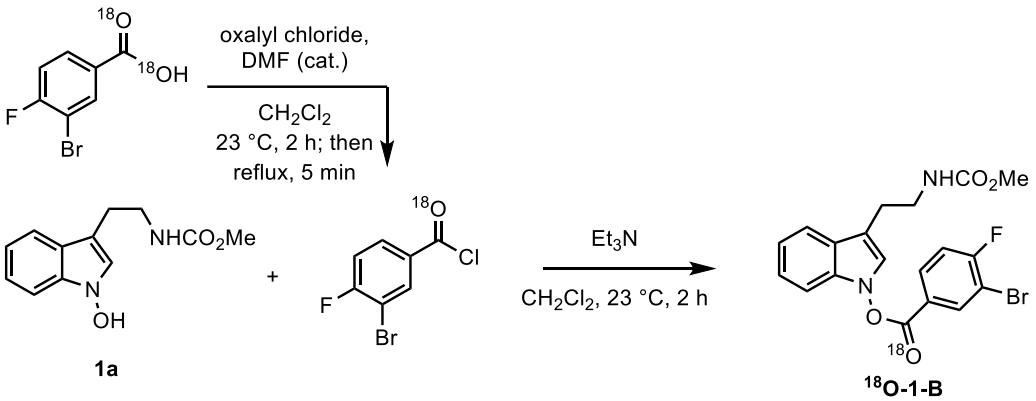
^{18}O-3-Bromo-4-fluorobenzoic acid



To an oven-dried heavy-wall pressure tube equipped with a stir bar and rubber septum were added 3-bromo-4-fluorobenzotrichloride (0.230 g, 0.787 mmol, 1.0 equiv) and $H_2{}^{18}O$ (160 μL, 7.99 mmol, 10.2 equiv) at 23 °C. The rubber septum was replaced with a Teflon screw cap under N_2 and the resulting mixture was heated to 120 °C in a pre-heated oil bath and stirred for 24 h. After the reaction mixture was cooled to 23 °C, the white solid was formed and precipitate was collected by filtration. The resulting filter cake was washed with H_2O (1 × 3 mL), and the solid was dried *in vacuo*, to afford ^{18}O-3-bromo-4-fluorobenzoic acid (70.8 mg, 40%) as a white solid. The resulting residue was used directly in the subsequent reaction without further purification. Analytic data is in agreement with the reported literature values.

***R*$_f$**=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.35 (dd, *J* = 6.6, 2.1 Hz, 1H), 8.07 (ddd, *J* = 8.6, 4.7, 2.1 Hz, 1H), 7.22 (t, *J* = 8.3 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 169.9, 162.8 (d, *J* = 256.3 Hz), 136.2 (d, *J* = 1.8 Hz), 131.7 (d, *J* = 8.7 Hz), 126.8 (d, *J* = 3.6 Hz), 116.9 (d, *J* = 23.1 Hz), 109.7 (d, *J* = 21.8 Hz); **^{19}F NMR** (471 MHz, $CDCl_3$): δ –98.1 (dd, *J* = 12.4, 6.7 Hz); **HRMS** calcd. for $C_7H_3BrF^{18}O_2^-$ $[M - H]^-$ 220.9391, found 220.9391; **Isotopic Incorporation:** [M+4] 96.6%, [M+2] 3.4%, [M+0] 0.0%.

3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl 3-bromo-4-fluorobenzoate (^{18}O-1-B)



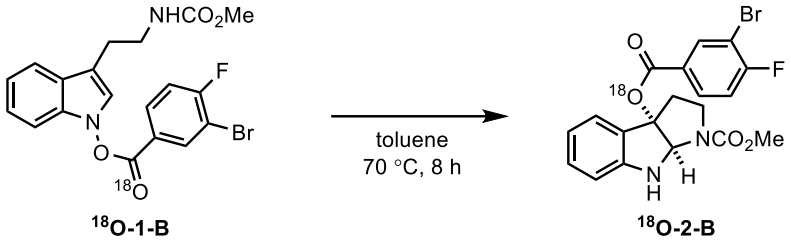
To an oven-dried two-neck round-bottom flask equipped with a stir bar, septum, and condenser were added ^{18}O-3-bromo-4-fluorobenzoic acid (70.8 mg, 0.317 mmol, 1.0 equiv) and CH_2Cl_2 (3 mL) at 23 °C, followed by DMF (a few drops) and oxalyl chloride (136 μL, 1.59 mmol, 5.0 equiv). The reaction mixture was stirred for 2 h at 23 °C, then heated to reflux in a pre-heated oil bath and stirred for additional 5 min before it was directly concentrated under reduced pressure. The resulting ^{18}O-benzoyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1a** (72.9 mg, 0.311 mmol, 1.0 equiv) and CH_2Cl_2 (10 mL) at 23 °C, followed by the crude benzoyl chloride and Et_3N (56 μL, 0.402 mmol, 1.3 equiv). The resulting mixture was stirred for 2 h, before it was cooled to 23 °C and quenched with H_2O (10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (107 mg, 79%) as a pale pink oil.

***R**f*=0.70 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.47 (dd, *J* = 6.5, 2.2 Hz, 1H), 8.18 (ddd, *J* = 8.7, 4.7, 2.2 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.35 – 7.20 (m, 5H), 7.10 (s, 1H), 4.89 (s, 1H), 3.70 (s, 3H), 3.56 (q, *J* = 6.7 Hz, 2H), 2.99 (t, *J* = 6.9 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.2 (d, *J* = 257.8 Hz), 162.9, 157.2, 136.2, 136.1 (d, *J* = 2.1 Hz), 131.6 (d, *J* = 8.8 Hz), 125.2, 124.3, 124.1 (d, *J* = 3.7 Hz), 123.8, 121.4, 119.5, 117.3 (d, *J* = 23.1 Hz), 112.8, 110.3 (d, *J* = 21.9 Hz), 109.3, 52.2, 41.0, 25.9; **^{19}F NMR** (471 MHz, $CDCl_3$): δ –98.1; **HRMS** calcd. for $C_{19}H_{17}BrFN_2O_3{}^{18}O^+$ $[M + H]^+$ 437.0393, found 437.0388; **Isotopic Incorporation:**

[M+2] 89.5%, [M+0] 11.5%.

Methyl 3a-((3-bromo-4-fluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-B)



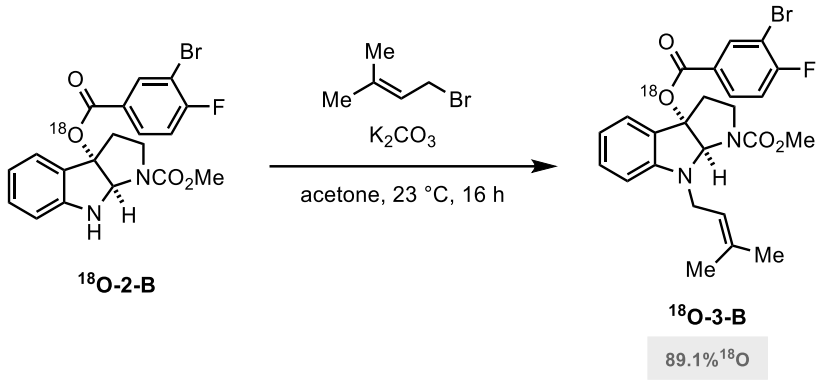
^{18}O-1-B ^{18}O-2-B

89.7%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-1-B** (80.0 mg, 0.183 mmol, 1.0 equiv) and toluene (4 mL) at 23 °C. The resulting mixture was heated to 70 °C in a pre-heated oil bath and stirred for 8 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The resulting residue was purified directly by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (47.3 mg, 59%) as a pale pink oil.

***R*$_f$**=0.70 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.20 (dd, *J* = 6.6, 2.1 Hz, 1H), 7.95 – 7.88 (m, 1H), 7.60 and 7.54 (d, *J* = 7.5 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.14 (t, *J* = 8.3 Hz, 1H), 6.80 (q, *J* = 6.9 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 5.75 (d, *J* = 3.5 Hz, 1H), 3.93 and 3.81 (t, *J* = 9.7 Hz, 1H), 3.80 and 3.73 (s, 2H), 3.22 (ddd, *J* = 17.2, 8.5, 4.9 Hz, 1H), 3.07 and 2.98 (dd, *J* = 12.8, 6.2 Hz, 1H), 2.69 (tdd, *J* = 12.0, 8.7, 3.2 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.4, 163.3, 155.7, 151.1, 150.8, 135.6, 131.4, 131.1 (d, *J* = 8.5 Hz), 127.9, 127.8, 126.7, 126.2, 125.5, 119.8, 119.6, 116.6 (d, *J* = 23.0 Hz), 110.5, 110.4, 109.4 (d, *J* = 21.7 Hz), 95.1, 93.8, 80.4, 79.6, 53.0, 52.7, 45.6, 35.8, 35.7; **^{19}F NMR** (471 MHz, $CDCl_3$): δ –99.3 (q, *J* = 7.1 Hz), –99.4 (q, *J* = 7.2 Hz); **HRMS** calcd. for $C_{19}H_{17}BrFN_2O_3{}^{18}O^+$ $[M + H]^+$ 437.0393, found 437.0397; **Isotopic Incorporation:** [M+2] 89.7%, [M+0] 11.3%.

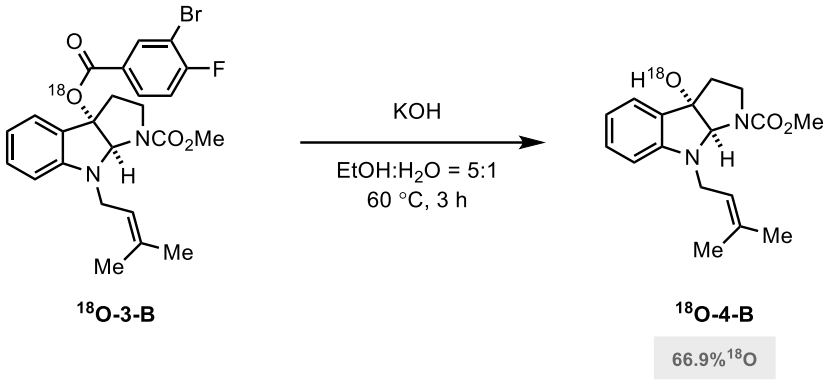
Methyl 3a-((3-bromo-4-fluorobenzoyl)oxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-B)



To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-2-B** (47.3 mg, 0.108 mmol, 1.0 equiv) and acetone (5 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (19 μL, 0.162 mmol, 1.5 equiv) and K_2CO_3 (44.2 mg, 0.320 mmol, 3.0 equiv). The resulting mixture was stirred for 16 h, before it was directly concentrated under reduced pressure and re-dissolved in CH_2Cl_2 (5 mL) and H_2O (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (44.9 mg, 82%) as a pale pink oil.

***R**$_f$*=0.50 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$, 55:45 mixture of rotamers): δ 8.18 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.93 (ddd, *J* = 8.8, 4.8, 2.2 Hz, 1H), 7.49 and 7.44 (s, 1H), 7.21 (td, *J* = 7.8, 1.3 Hz, 1H), 7.14 (t, *J* = 8.4 Hz, 1H), 6.71 (t, *J* = 7.4 Hz, 1H), 6.54 (br s, 1H), 5.87 and 5.80 (s, 1H), 5.23 (t, *J* = 6.2 Hz, 1H), 4.29 – 4.19 (m, 1H), 4.12 – 4.00 (m, 2H), 3.97 – 3.90 (m, 1H), 3.78 and 3.75 (s, 3H), 3.16 (br s, 1H), 2.91 – 2.76 (m, 1H), 2.64 (td, *J* = 12.1, 8.4 Hz, 1H), 1.78 (d, *J* = 12.9 Hz, 3H), 1.72 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.3, 163.2, 161.3, 155.9, 155.1, 152.1, 135.6 (d, *J* = 1.1 Hz), 135.0, 134.5, 131.3, 131.1 (d, *J* = 8.4 Hz), 128.0, 126.5, 126.3, 126.0, 125.5, 121.1, 120.8, 118.3, 116.6 (d, *J* = 23.0 Hz), 109.4 (d, *J* = 21.8 Hz), 108.4, 108.0, 95.3, 94.3, 84.9, 84.3, 52.8, 45.4, 45.2, 45.0, 37.7, 37.6, 26.0, 18.3; **^{19}F NMR** (471 MHz, $CDCl_3$): δ –99.4, –99.5; **HRMS** calcd. for $C_{24}H_{25}BrFN_2O_3{}^{18}O^+$ $[M + H]^+$ 505.1019, found 505.1017; **Isotopic Incorporation:** [M+2] 89.1%, [M+0] 11.9%.

Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-B)



^{18}O-3-B **^{18}O-4-B**

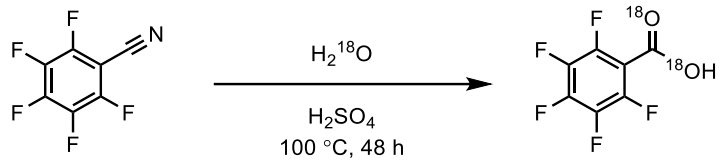
66.9%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-3-B** (44.9 mg, 0.089 mmol, 1.0 equiv) and EtOH: H_2O (5:1, 6 mL) at 23 °C, followed by KOH (7.5 mg, 0.134 mmol, 1.5 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and diluted with CH_2Cl_2 (5 mL) and H_2O (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (19.1 mg, 71%) as a pale yellow oil.

***R**$_f$*=0.44 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 50:50 mixture of rotamers): δ 7.25 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.49 (s, 1H), 5.38 and 5.30 (s, 1H), 5.16 (s, 1H), 4.22 – 4.08 and 4.07 – 3.93 (m, 1H), 4.07 – 3.93 (m, 1H), 4.07 – 3.93 and 3.87 – 3.79 (m, 1H), 3.73 (s, 3H), 3.23 – 3.04 (m, 2H), 2.41 – 2.23 (m, 2H), 1.75 (d, *J* = 11.7 Hz, 3H), 1.69 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.4, 135.2, 130.8, 130.7, 130.5, 123.4, 123.2, 120.4, 120.3, 118.2, 108.4, 108.0, 87.7, 87.5, 86.9, 52.7, 45.8, 44.9, 44.4, 38.4, 25.9, 18.3; **HRMS** calcd. for $C_{17}H_{23}N_2O_2{}^{18}O^+$ $[M + H]^+$ 305.1746, found 305.1740; **Isotopic Incorporation:** [M+2] 66.9%, [M+0] 33.1%.

3.2.1.3. Pentafluorobenzoyl substituent

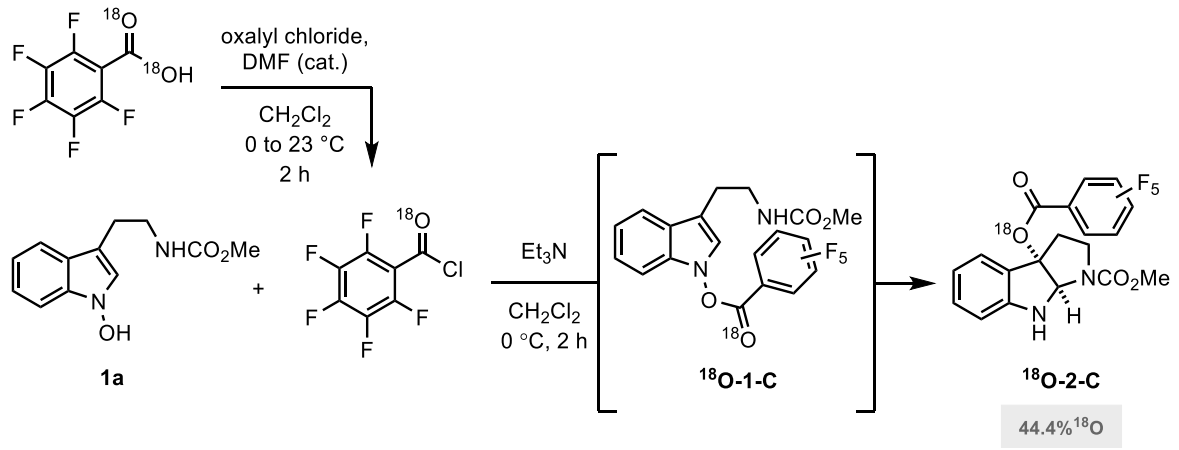
^{18}O-2,3,4,5,6-Pentafluorobenzoic acid



To an oven-dried heavy-wall pressure tube equipped with a stir bar and rubber septum were added 2,3,4,5,6-pentafluorobenzonitrile (965 mg, 5.00 mmol, 1.0 equiv) and sulfuric acid (0.5 mL) at 23 °C, followed by $H_2{}^{18}O$ (500 μL, 25.0 mmol, 5.0 equiv). The rubber septum was replaced with a Teflon screw cap under N_2 and the resulting mixture was heated to 100 °C in a pre-heated oil bath. The reaction mixture was stirred for 48 h and cooled to 23 °C before it was diluted with CH_2Cl_2 (20 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford ^{18}O-pentafluorobenzoic acid (248 mg, 23%) as a white-beige solid. The resulting residue was used directly in the subsequent reaction without further purification.

***R**$_f$* = 0.10 (silica gel, hexanes:EtOAc = 9:1); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 164.0, 147.6 – 145.2 (dm, *J* = 263.1 Hz), 145. 5 – 143.0 (dm, d, *J* = 256.3 Hz), 139.2 – 136.7 (dm, d, *J* = 256.5 Hz), 106.8 (td, *J* = 14.4, 4.1 Hz); **^{19}F NMR** (471 MHz, $CDCl_3$): δ −136.2 (dt, *J* = 19.5, 5.5 Hz), −146.1 (td, *J* = 20.9, 5.9 Hz), −159.8 – −159.9 (m); **HRMS** calcd. for $C_7F_5{}^{18}O_2{}^-$ [M – H]$^-$ 214.9909, found 214.9910; **Isotopic Incorporation:** [M+4] 19.5%, [M+2] 49.6%, [M+0] 30.9%.

Methyl 3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-C)



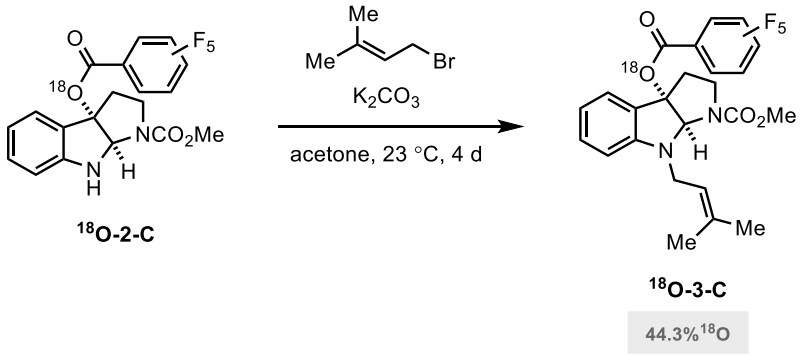
To an oven-dried round-bottom flask equipped with a stir bar and septum were added ^{18}O-2,3,4,5,6-pentafluorobenzoic acid (50 mg, 0.231 mmol, 1.04 equiv) and CH_2Cl_2 (3 mL) at 23 °C. The resulting solution was cooled to 0 °C, and DMF (a few drops) and oxalyl chloride (19 μL, 0.222 mmol, 1.0 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was directly concentrated under reduced pressure. The resulting ^{18}O-benzoyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1a** (51.5 mg, 0.220 mmol, 1.0 equiv) and CH_2Cl_2 (5 mL) at 23 °C. The solution was then cooled to 0 °C and the crude benzoyl chloride and Et_3N (40 μL, 0.287 mmol, 1.3 equiv) was added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was quenched with H_2O (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (45.2 mg, 47%) as a pale yellow oil.

***R**$_f$*=0.56 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.56 and 7.53 (d, *J* = 8.7 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 6.83 (q, *J* = 7.2, 6.7 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.71 (d, *J* = 3.3 Hz, 1H), 3.92 and 3.82 (t, *J* = 9.7 Hz, 1H), 3.80 and 3.73 (s, 3H), 3.25 – 3.16 (m, 1H), 3.03 and 2.96 (dd, *J* = 12.6, 6.2 Hz, 1H), 2.70 (q, *J* = 10.7 Hz, 1H) ; **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.8, 155.6, 154.8, 151.2, 151.0, 147.2 – 144.0 (dm, *J* = 262.7 Hz), 145.1 – 141.9 (dm, *J* = 260.2 Hz), 139.5 – 136.1 (dm, *J* = 257.6 Hz),

131.7, 126.4, 126.1, 124.8, 124.7, 122.6, 120.5, 120.0, 119.7, 110.7, 110.5, 108.2 (t, J = 15.7 Hz), 96.6, 95.4, 80.1, 79.4, 53.0, 52.8, 45.5, 35.7, 35.6; **^{19}F NMR** (376 MHz, $CDCl_3$): δ δ −139.6 (dp, J = 17.0, 5.8 Hz), −149.6 (dtt, J = 57.4, 20.7, 4.8 Hz), −161.8 – −162.0 (m); **HRMS** calcd. for $C_{19}H_{14}F_5N_2O_3{}^{18}O^+$ $[M + H]^+$ 431.0911, found 431.0907; **Isotopic Incorporation:** [M+2] 44.4%, [M+0] 55.6%.

Methyl 8-(3-methylbut-2-en-1-yl)-3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-C)



^{18}O-2-C

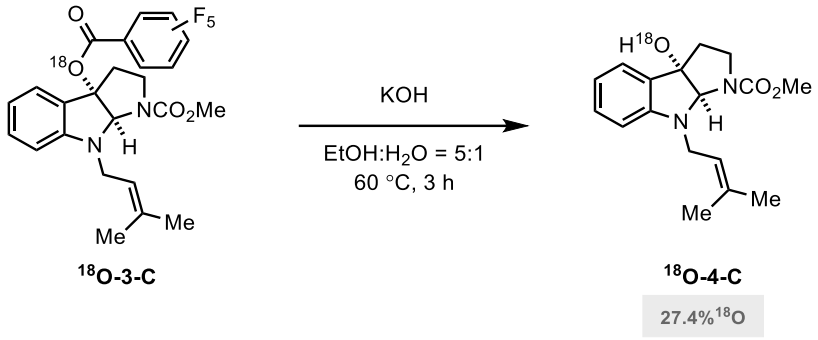
^{18}O-3-C

44.3%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-2-C** (45.2 mg, 0.105 mmol, 1.0 equiv) and acetone (3 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (37 μL, 0.315 mmol, 3.0 equiv) and K_2CO_3 (87.0 mg, 0.629 mmol, 6.0 equiv). The resulting mixture was stirred for 4 d, before it was directly concentrated under reduced pressure and re-dissolved in CH_2Cl_2 (5 mL) and H_2O (5mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (43.1 mg, 82%) as a pale yellow oil.

***R**$_f$*=0.66 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.46 (d, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.9 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.53 (d, *J* = 7.7 Hz, 1H), 5.83 and 5.76 (s, 1H), 5.20 (s, 1H), 4.27 – 4.23 and 4.10 – 4.08 (m, 1H), 4.05 – 3.89 (m, 3H), 3.78 and 3.75 (s, 3H), 3.26 – 3.06 (m, 1H), 2.92 – 2.75 (m, 1H), 2.72 – 2.56 (m, 1H), 1.76 (s, 3H), 1.69 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.6, 155.8, 155.0, 152.1, 146.9 – 144.4 (dm, *J* = 264.7 Hz), 144.6 – 142.0 (dm, *J* = 260.6 Hz), 139.2 – 136.4 (dm, *J* = 250.5 Hz), 135.2, 134.7, 131.6, 128.2, 125.7, 125.6, 120.9, 120.5, 118.6, 108.7, 108.3, 97.0, 95.9, 84.7, 84.2, 52.9, 45.6, 45.5, 45.1, 44.9, 38.2, 37.6, 37.6, 25.8, 18.2; **^{19}F NMR** (471 MHz, $CDCl_3$): δ −137.4 (dq, *J* = 17.5, 5.8 Hz), −137.8 (tdd, *J* = 26.9, 12.3, 7.0 Hz), −148.0 (dt, *J* = 43.5, 20.8 Hz), −148.2 (ddd, *J* = 25.5, 13.0, 4.7 Hz), −160.2 – −160.3 (m), −160.4 – −160.5 (m); **HRMS** calcd. for $C_{24}H_{22}F_5N_2O_3{}^{18}O^+$ $[M + H]^+$ 499.1537, found 499.1535; **Isotopic Incorporation:** [M+2] 44.3%, [M+0] 55.7%.

Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-4-C)

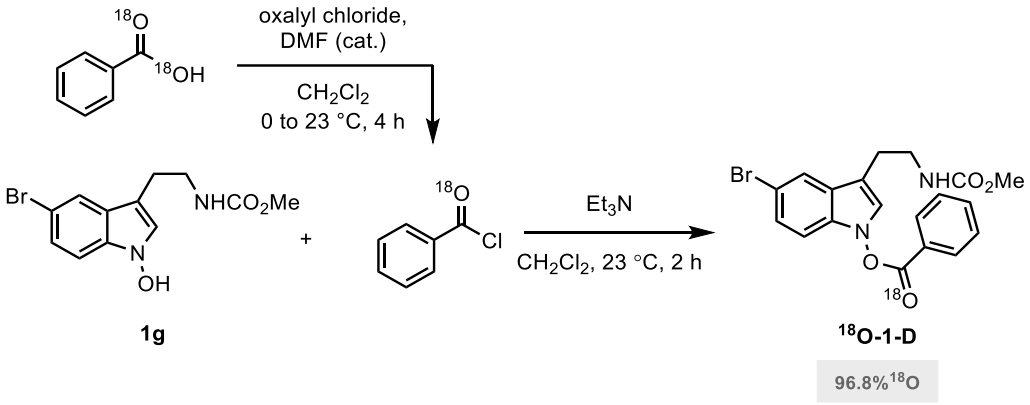


To an oven-dried round-bottom flask equipped with a stir bar and septum were added **18O-3-C** (43.1 mg, 0.086 mmol, 1.0 equiv) and EtOH: H_2O (5:1, 4 mL) at 23 °C, followed by KOH (7.0 mg, 0.125 mmol, 1.5 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and diluted with CH_2Cl_2 (5 mL) and H_2O (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (18.1 mg, 69%) as a pale yellow oil.

***R**f*=0.45 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 50:50 mixture of rotamers): δ 7.25 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.49 (s, 1H), 5.38 and 5.30 (s, 1H), 5.16 (s, 1H), 4.22 – 4.08 and 4.07 – 3.93 (m, 1H), 4.07 – 3.93 (m, 1H), 4.07 – 3.93 and 3.87 – 3.79 (m, 1H), 3.73 (s, 3H), 3.23 – 3.04 (m, 2H), 2.41 – 2.23 (m, 2H), 1.75 (d, *J* = 11.7 Hz, 3H), 1.69 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.4, 135.2, 130.8, 130.7, 130.5, 123.4, 123.2, 120.4, 120.3, 118.2, 108.4, 108.0, 87.7, 87.5, 86.9, 52.7, 45.8, 44.9, 44.4, 38.4, 25.9, 18.3; **HRMS** calcd. for $C_{17}H_{23}N_2O_2{}^{18}O^+$ $[M + H]^+$ 305.1746, found 305.1740; **Isotopic Incorporation:** [M+2] 27.4%, [M+0] 72.6%.

3.2.1.4. Bromotryptamine with benzoyl substituent

5-Bromo-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (^{18}O-1-D)

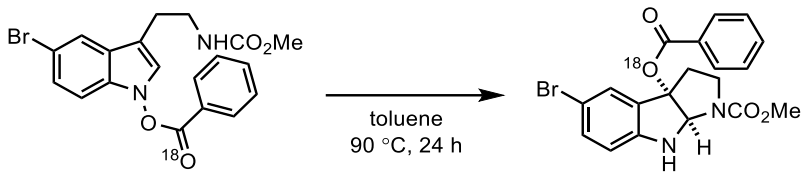


To an oven-dried two-neck round-bottom flask equipped with a stir bar, septum, and condenser were added ^{18}O-benzoic acid (31.8 mg, 0.252 mmol, 1.02 equiv), DMF (a few drops) and CH_2Cl_2 (3 mL) at 23 °C. The resulting solution was cooled to 0 °C and oxalyl chloride (32 μL, 0.371 mmol, 1.5 equiv) was added dropwise. The reaction mixture was stirred for 4 h at 23 °C, before it was directly concentrated under reduced pressure. The resulting ^{18}O-benzoyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1g** (77.3 mg, 0.247 mmol, 1.0 equiv) and CH_2Cl_2 (10 mL) at 23 °C, followed by the crude benzoyl chloride and Et_3N (44 μL, 0.317 mmol, 1.3 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H_2O (10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (68.6 mg, 66%) as a pale yellow oil.

***R**f*=0.48 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.1 Hz, 2H), 7.76 – 7.68 (m, 1H), 7.73 (s, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 2H), 7.10 (s, 1H), 3.69 (s, 3H), 3.51 (q, *J* = 6.7 Hz, 2H), 2.94 (t, *J* = 6.8 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 164.7, 157.2, 134.9, 134.1, 130.4, 130.3, 129.2, 128.6, 126.5, 126.2, 125.0, 122.1, 114.2, 110.6, 52.3, 41.2, 25.7; **HRMS** calcd. for $C_{19}H_{18}BrN_2O_3{}^{18}O^+$ $[M + H]^+$ 419.0487, found 419.0496; **Isotopic Incorporation:** [M+2] 96.8%, [M+0] 3.2%.

Methyl 3a-(benzoyloxy)-5-bromo-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-D)



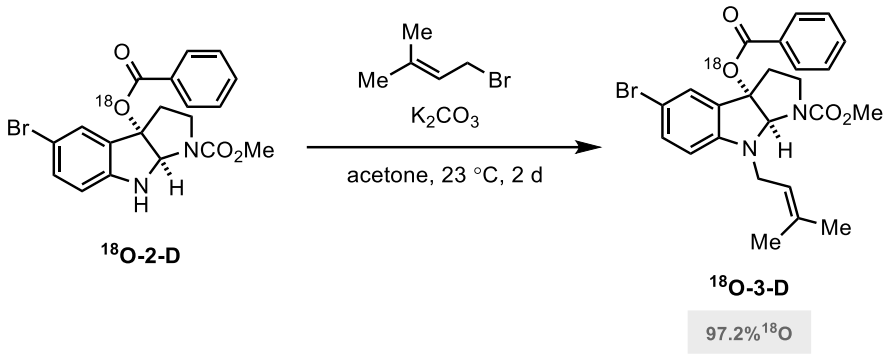
^{18}O-1-D **^{18}O-2-D**

97.1%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-1-D** (68.6 mg, 0.164 mmol, 1.0 equiv) and toluene (3 mL) at 23 °C. The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 24 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The resulting residue was purified directly by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (34.5 mg, 50%) as a pale yellow oil.

***R**$_f$*=0.48 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.99 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.72 and 7.63 (s, 1H), 7.56 (td, *J* = 7.6, 3.8 Hz, 2H), 7.43 (td, *J* = 7.9, 2.3 Hz, 1H), 7.30 – 7.26 (m, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 5.77 (s, 1H), 5.25 and 4.91 (s, 1H), 3.93 and 3.82 (t, *J* = 9.2 Hz, 1H), 3.79 and 3.73 (s, 3H), 3.24 (td, *J* = 10.9, 6.4 Hz, 1H), 3.01 and 2.90 (ddd, *J* = 12.9, 6.4, 1.8 Hz, 2H), 2.70 (ddd, *J* = 12.9, 10.9, 8.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.4, 155.7, 154.8, 150.0, 149.7, 133.9, 133.6, 133.5, 129.9, 129.5, 128.9, 128.6, 128.3, 128.1, 111.8, 111.7, 111.2, 110.9, 94.0, 92.7, 80.7, 79.9, 53.0, 52.8, 45.5, 45.4, 36.1, 35.9; **HRMS** calcd. for $C_{19}H_{18}BrN_2O_3{}^{18}O^+$ $[M + H]^+$ 419.0487, found 419.0494; **Isotopic Incorporation:** [M+2] 97.1%, [M+0] 2.9%.

Methyl 3a-(benzoyloxy)-5-bromo-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-D)



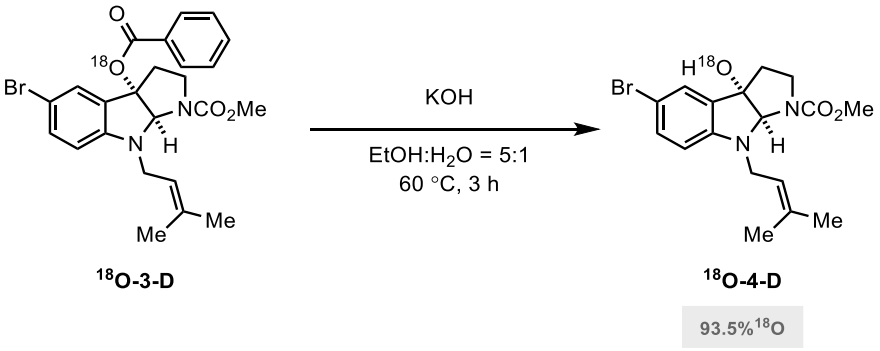
^{18}O-2-D **^{18}O-3-D**

97.2%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-2-D** (34.5 mg, 0.082 mmol, 1.0 equiv) and acetone (4 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (28 μL, 0.246 mmol, 3.0 equiv) and K_2CO_3 (67.7 mg, 0.490 mmol, 6.0 equiv). The resulting mixture was stirred for 2 d, before it was directly concentrated under reduced pressure and re-dissolved in CH_2Cl_2 (5 mL) and H_2O (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (29.0 mg, 73%) as a pale yellow oil.

***R**$_f$*=0.69 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$, 50:50 mixture of rotamers): δ 7.98 (d, *J* = 7.6 Hz, 1H), 7.63 – 7.48 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 2.1 Hz, 2H), 6.40 and 6.39 (s, 1H), 5.90 and 5.84 (s, 1H), 5.21 (s, 1H), 4.26 – 4.21 and 4.14 – 4.07 (m, 1H), 4.04 – 3.92 (m, 2H), 3.75 (s, 3H), 3.23 – 3.08 (m, 1H), 2.87 – 2.71 (m, 1H), 2.65 (q, *J* = 11.2, 10.5 Hz, 1H), 1.76 (d, *J* = 13.0 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): 165.2, 151.0, 133.7, 133.5, 130.1, 129.9, 129.1, 129.0, 128.5, 120.7, 120.5, 109.7, 109.5, 109.3, 93.9, 92.9, 85.2, 84.6, 52.9, 45.5, 45.2, 44.8, 37.8, 25.9, 18.2; **HRMS** calcd. for $C_{24}H_{26}BrN_2O_3{}^{18}O^+$ $[M + H]^+$ 487.1113, found 487.1107; **Isotopic Incorporation:** [M+2] 97.2%, [M+0] 2.8%.

Methyl 5-bromo-3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-D)

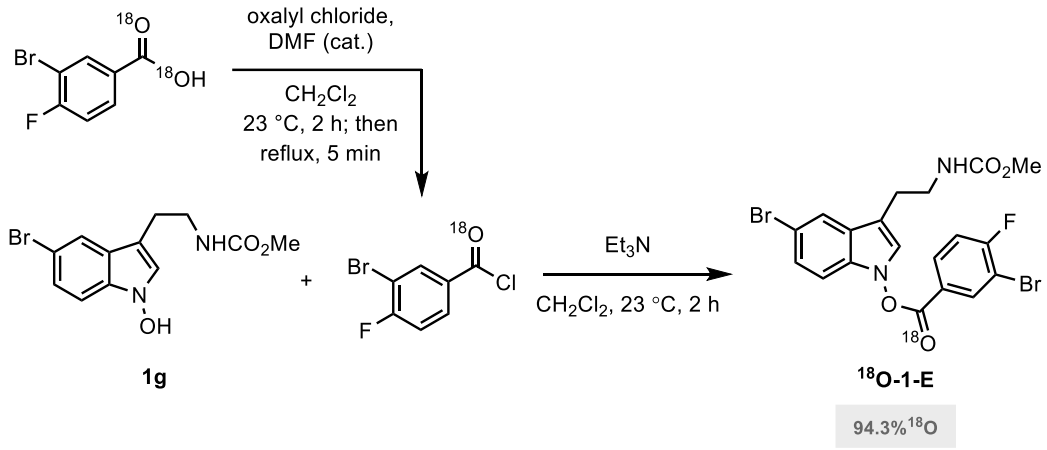


To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-3-D** (29.0 mg, 0.060 mmol, 1.0 equiv) and EtOH: H_2O (5:1, 3 mL) at 23 °C, followed by KOH (5.0 mg, 0.090 mmol, 1.5 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and diluted with CH_2Cl_2 (2 mL) and H_2O (2 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layer was washed with brine (1 × 3 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (15.0 mg, 65%) as a pale yellow oil.

***R**$_f$*=0.55 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 55:45 mixture of rotamers): δ 7.32 (d, *J* = 2.1 Hz, 1H), 7.27 (d, *J* = 2.1 Hz, 1H), 6.35 (t, *J* = 8.1 Hz, 1H), 5.39 and 5.31 (s, 1H), 5.13 and 5.09 (s, 1H), 4.16 – 4.10 and 3.99 – 3.96 (m, 1H), 3.96 – 3.83 (m, 3H), 3.73 (s, 3H), 3.25 – 3.05 (m, 2H), 2.39 – 2.22 (m, 2H), 1.74 (d, *J* = 14.0 Hz, 3H), 1.69 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 149.3, 135.7, 135.4, 133.4, 133.3, 126.5, 126.4, 119.9, 119.8, 109.8, 109.5, 88.3, 87.8, 87.1, 52.8, 45.8, 44.8, 44.3, 38.5, 25.9; **HRMS** calcd. for $C_{17}H_{22}BrN_2O_2{}^{18}O^+$ $[M + H]^+$ 383.0851, found 383.0838; **Isotopic Incorporation:** [M+2] 93.5%, [M+0] 6.5%.

3.2.1.5. Bromotryptamine with 3-bromo-4-fluorobenzoyl substituent

5-Bromo-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indol-1-yl 3-bromo-4-fluorobenzoate (^{18}O-1-E)



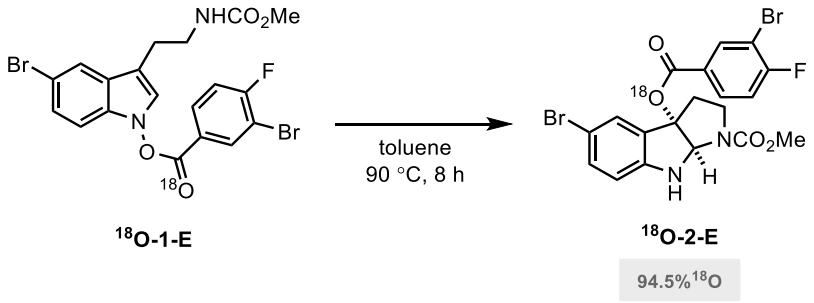
To an oven-dried two-neck round-bottom flask equipped with a stir bar, septum, and a reflux condenser were added ^{18}O-3-bromo-4-fluorobenzoic acid (60.0 mg, 0.269 mmol, 1.04 equiv) and CH_2Cl_2 (3 mL) at 23 °C, followed by DMF (a few drops) and oxalyl chloride (111 μL, 1.29 mmol, 5.0 equiv). The reaction mixture was stirred for 2 h at 23 °C, then heated to reflux in a pre-heated oil bath and stirred for additional 5 min before it was directly concentrated under reduced pressure. The resulting ^{18}O-benzoyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1g** (80.8 mg, 0.258 mmol, 1.0 equiv) and CH_2Cl_2 (10 mL) at 23 °C, followed by the crude benzoyl chloride and Et_3N (47 μL, 0.337 mmol, 1.3 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H_2O (10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was washed with brine (1 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (77.2 mg, 58%) as a pale yellow oil.

***R**$_f$*=0.55 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.43 (dd, *J* = 6.5, 2.2 Hz, 1H), 8.16 (ddd, *J* = 8.6, 4.6, 2.2 Hz, 1H), 7.73 (d, *J* = 1.8 Hz, 1H), 7.34 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.31 (t, *J* = 8.3 Hz, 1H), 7.10 (d, *J* = 8.6 Hz, 1H), 7.08 (s, 1H), 4.80 (s, 1H), 3.68 (s, 3H), 3.51 (q, *J* = 6.8 Hz, 2H), 2.93 (t, *J* = 6.8 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.3 (d, *J* = 258.2 Hz), 162.8, 157.2, 136.2, 134.4, 131.7 (d, *J* = 8.9 Hz), 126.7, 125.1, 123.8 (d, *J* = 3.8 Hz), 122.2, 117.5, 117.4 (d, *J* = 23.2 Hz), 117.4, 114.5, 111.9, 110.6, 110.5, 110.3, 52.3,

41.1, 25.7; **^{19}F NMR** (471 MHz, $CDCl_3$): δ −95.8 (dd, J = 12.5, 5.7 Hz); **HRMS** calcd. for $C_{19}H_{15}Br_2FN_2O_3{}^{18}ONa^+$ $[M + Na]^+$ 536.9317, found 536.9327; **Isotopic Incorporation:** [M+2] 94.3%, [M+0] 5.7%.

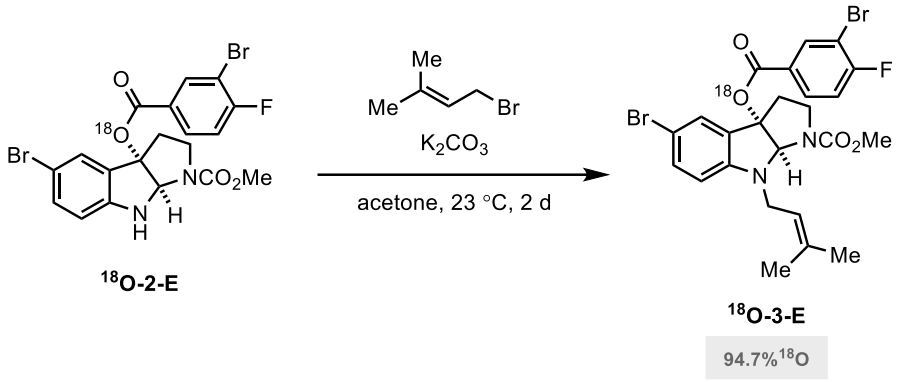
Methyl 5-bromo-3a-((3-bromo-4-fluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-E)



To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-1-E** (77.2 mg, 0.150 mmol, 1.0 equiv) and toluene (3 mL) at 23 °C. The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 8 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The resulting residue was purified directly by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (42.6 mg, 55%) as a pale yellow oil.

***R*$_f$**=0.55 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.20 (dt, *J* = 6.5, 1.8 Hz, 1H), 7.98 – 7.89 (m, 1H), 7.69 and 7.63 (s, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.16 (t, *J* = 8.5 Hz, 1H), 6.57 (dd, *J* = 8.4, 1.4 Hz, 1H), 5.74 (d, *J* = 1.8 Hz, 1H), 5.27 and 4.91 (s, 1H), 3.93 and 3.82 (t, *J* = 9.8 Hz, 1H), 3.79 and 3.73 (s, 3H), 3.23 (q, *J* = 11.9, 10.8 Hz, 1H), 3.02 and 2.93 (dd, *J* = 13.2, 6.1 Hz, 1H), 2.67 (q, *J* = 10.9 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.3, 162.4 (d, *J* = 254.9 Hz), 155.6, 154.7, 150.0, 149.8, 135.7, 134.1, 131.18 (d, *J* = 8.6 Hz), 129.5, 129.1, 127.7, 127.6, 127.5 (d, *J* = 3.4 Hz), 116.7 (d, *J* = 23.3 Hz), 111.9, 111.8, 111.2, 110.9, 109.6, 109.5, 94.4, 93.2, 80.6, 79.9, 53.1, 52.8, 45.5, 35.9, 35.8; **^{19}F NMR** (471 MHz, $CDCl_3$): δ –98.9 (q, *J* = 6.8 Hz), –99.0 (q, *J* = 6.9 Hz); **HRMS** calcd. for $C_{19}H_{16}Br_2FN_2O_3{}^{18}O^+$ $[M + H]^+$ 514.9498, found 514.9486; **Isotopic Incorporation:** [M+2] 94.5%, [M+0] 5.5%.

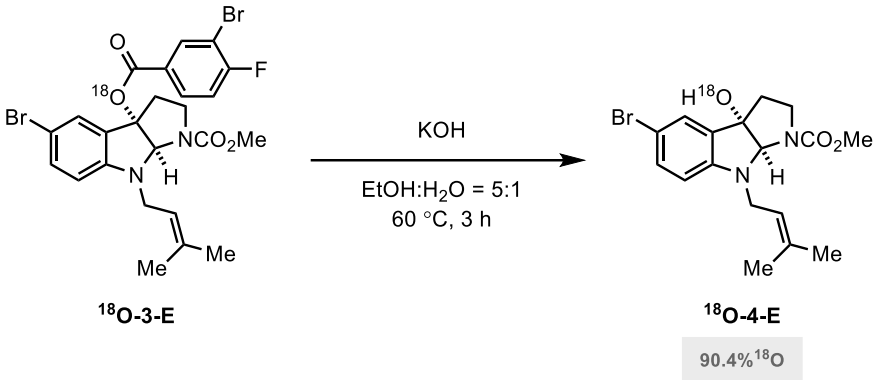
Methyl 5-bromo-3a-((3-bromo-4-fluorobenzoyl)oxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-E)



To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-2-E** (42.6 mg, 0.083 mmol, 1.0 equiv) and acetone (4 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (29 μL, 0.247 mmol, 3.0 equiv) and K_2CO_3 (69.0 mg, 0.499 mmol, 6.0 equiv). The resulting mixture was stirred for 2 d, before it was directly concentrated under reduced pressure and re-dissolved in CH_2Cl_2 (5 mL) and H_2O (5mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (34.3 mg, 71%) as a pale yellow oil.

***R**$_f$* =0.71 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.18 (d, *J* = 6.1 Hz, 1H), 7.93 (s, 1H), 7.57 and 7.50 (s, 1H), 7.28 (d, *J* = 8.7 Hz, 1H), 7.16 (t, *J* = 8.3 Hz, 1H), 6.40 and 6.39 (s, 1H), 5.88 and 5.80 (s, 1H), 5.19 (s, 1H), 4.23 and 4.04 (dd, *J* = 15.8, 6.8 Hz, 1H), 4.13 – 3.92 (m, 3H), 3.77 and 3.75 (s, 3H), 3.24 – 3.05 (m, 1H), 2.89 – 2.71 (m, 1H), 2.61 (q, *J* = 10.3 Hz, 1H), 1.77 (d, *J* = 10.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): 163.0, 162.3 (d, *J* = 255.6 Hz), 161.3, 150.9, 135.5, 133.8, 131.0 (d, *J* = 8.6 Hz), 128.5, 128.4, 127.6, 120.4, 120.3, 118.2, 116.5 (d, *J* = 23.1 Hz), 109.5, 109.3, 94.4, 93.4, 84.9, 84.2, 64.5, 52.7, 45.2, 44.9, 44.7, 37.8, 25.8, 18.1, 18.0; **^{19}F NMR** (471 MHz, $CDCl_3$): δ –99.0, –99.1; **HRMS** calcd. for $C_{24}H_{24}Br_2FN_2O_3{}^{18}O^+$ $[M + H]^+$ 583.0124, found 583.0116; **Isotopic Incorporation:** [M+2] 94.7%, [M+0] 5.3%.

Methyl 5-bromo-3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-E)



^{18}O-3-E **^{18}O-4-E**

90.4%^{18}O

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **^{18}O-3-E** (34.2 mg, 0.059 mmol, 1.0 equiv) and EtOH: H_2O (5:1, 2 mL) at 23 °C, followed by KOH (5.0 mg, 0.089 mmol, 1.5 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and diluted with CH_2Cl_2 (3 mL) and H_2O (3 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layer was washed with brine (1 × 3 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (15.6 mg, 69%) as a pale yellow oil.

***R**$_f$*=0.55 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 55:45 mixture of rotamers): δ 7.32 (d, *J* = 2.1 Hz, 1H), 7.27 (d, *J* = 2.1 Hz, 1H), 6.35 (t, *J* = 8.1 Hz, 1H), 5.39 and 5.31 (s, 1H), 5.13 and 5.09 (s, 1H), 4.16 – 4.10 and 3.99 – 3.96 (m, 1H), 3.96 – 3.83 (m, 3H), 3.73 (s, 3H), 3.25 – 3.05 (m, 2H), 2.39 – 2.22 (m, 2H), 1.74 (d, *J* = 14.0 Hz, 3H), 1.69 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 149.3, 135.7, 135.4, 133.4, 133.3, 126.5, 126.4, 119.9, 119.8, 109.8, 109.5, 88.3, 87.8, 87.1, 52.8, 45.8, 44.8, 44.3, 38.5, 25.9; **HRMS** calcd. for $C_{17}H_{22}BrN_2O_2{}^{18}O^+$ $[M + H]^+$ 383.0851, found 383.0820; **Isotopic Incorporation:** [M+2] 90.4%, [M+0] 9.6%.

3.2.2. Determination of ^{18}O Saturation

General information of HRMS

Reagents and Chemicals

MeCN (LC-MS grade), H_2O with 0.1% formic acid (LC-MS grade) were obtained from Samchun Chemical.

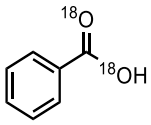
Instrumentation and Experimental

HRMS experiments were performed using a Thermo Scientific™ Orbitrap Exploris 120 equipped with a Hypersil GOLD™ C18 Selectivity HPLC column and Thermo Scientific™ mass spectrometer with Thermo Scientific™ Xcalibur™ software for instrument control and data processing. The aqueous mobile phase A is H_2O with 0.1% formic acid (v/v), and organic mobile phase B is MeCN with 0.1% formic acid (v/v). 20 μL of samples were injected onto the column with a flow rate of 0.4 mL/min at 40 °C. The chromatographic condition is as followed: 30 min method consisting with 5% B over 0.0–2.0 min, then a gradient of 5% B to 95% B over 2.0–20.0 min, then maintain 95% B over 20.0–24.9 min followed by a gradient of 95% B to 5% B over 24.9–25.0 min, then hold 5% B for 5 min. The eluents were monitored by a UV detector with a range of 210 nm to 400 nm, followed by HRMS detection in electrospray ionization with both positive and negative mode. The MS conditions were as followed: voltage for positive ion mode 3500 V, voltage for negative ion mode 3000 V, sheath gas flow rate 55 Arb; aux gas flow rate 15 Arb; sweep gas flow rate 1 Arb, ion transfer tube temperature 320 °C, vaporizer temperature 350 °C, orbitrap resolution 120000, m/z range 100–1000 Da.

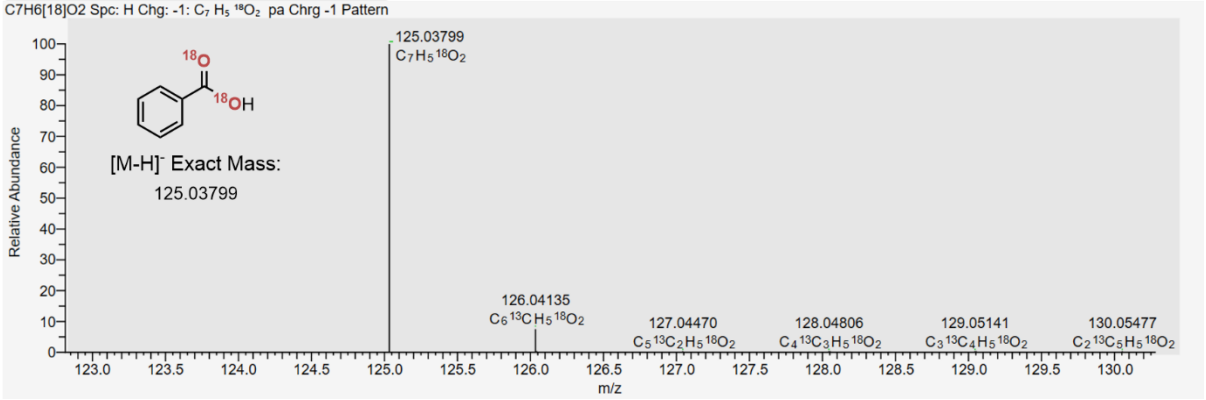
The conditions above were used for all the HRMS analysis in mechanistic section.

The M + 2 isotopic enrichment values (M = mass of unlabeled compound), and full isotopic incorporation data were calculated using the relative abundance in mass spectra for each M + n (n = 0, 2) peak in HRMS.

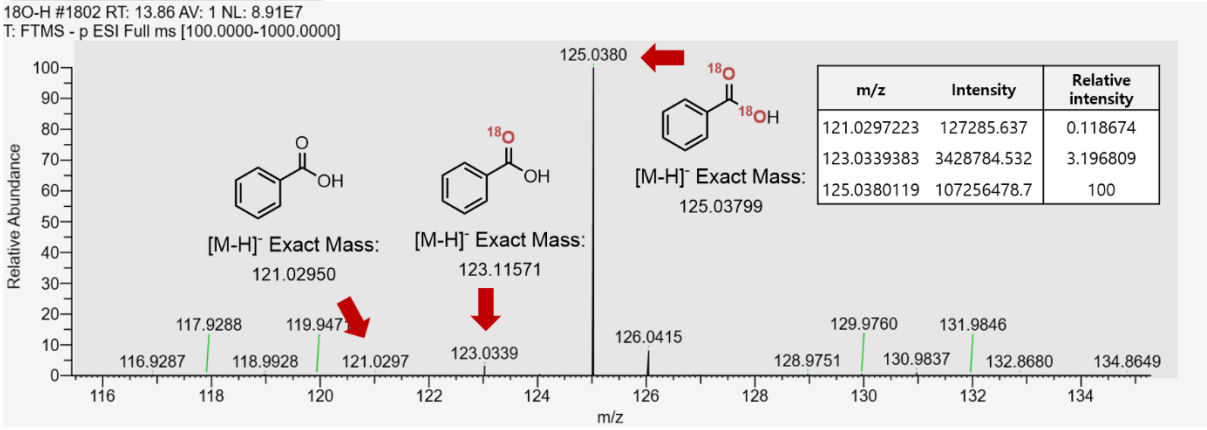
^{18}O-benzoic acid



Isotopic simulation of negative ion mode

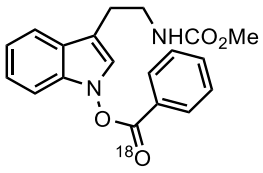


HRMS result of **^{18}O-benzoic acid**

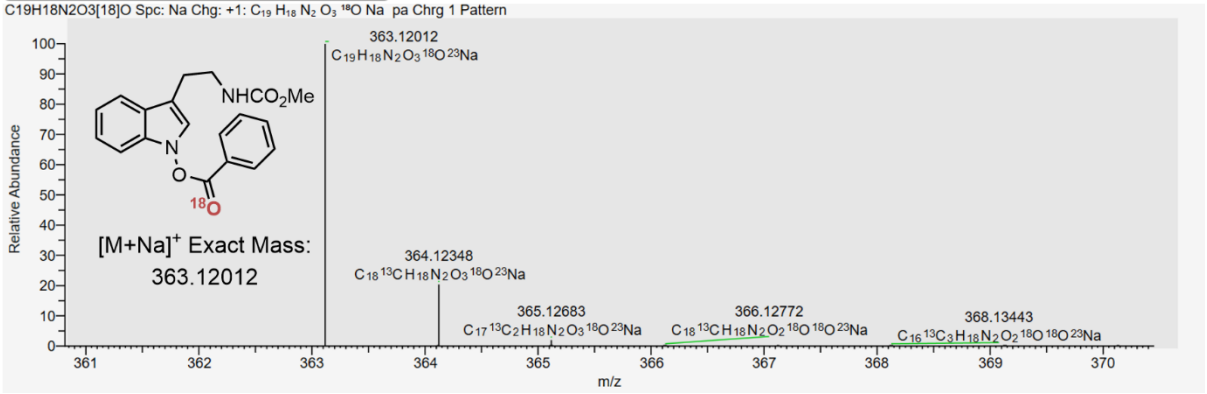


m/z	Intensity	Relative intensity
121.0297223	127285.637	0.118674
123.0339383	3428784.532	3.196809
125.0380119	107256478.7	100

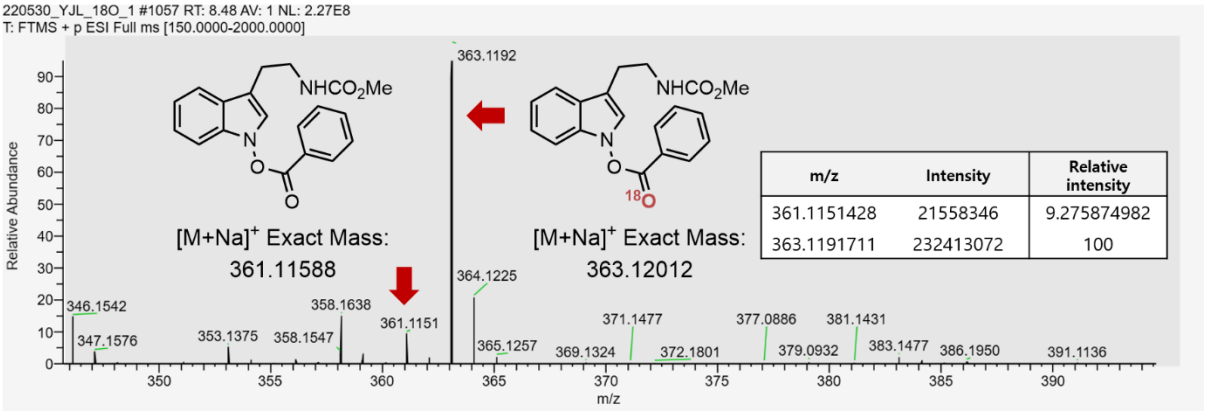
3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (^{18}O-1-A)



Isotopic simulation of positive ion mode



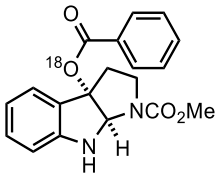
HRMS result of compound **^{18}O-1-A**



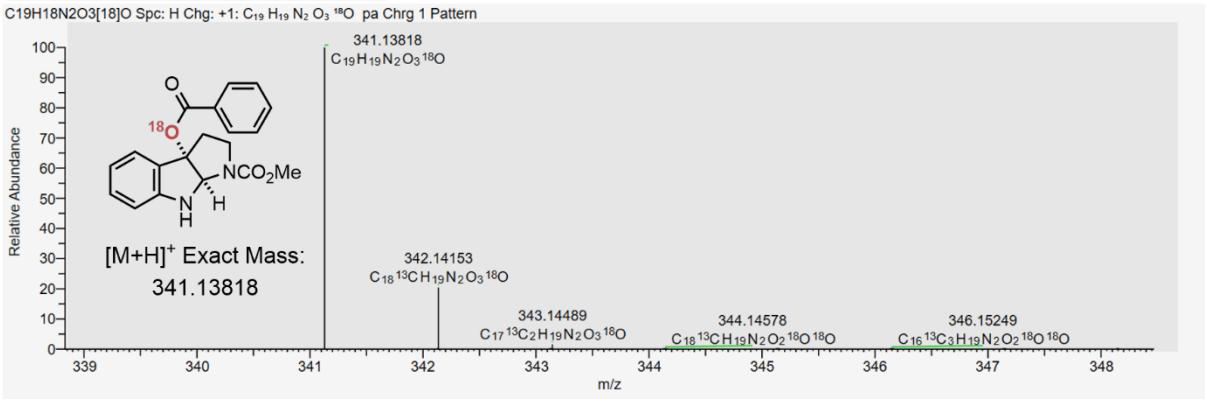
m/z	Intensity	Relative intensity
361.1151428	21558346	9.275874982
363.1191711	232413072	100

^{18}O enrichment: 91.5%

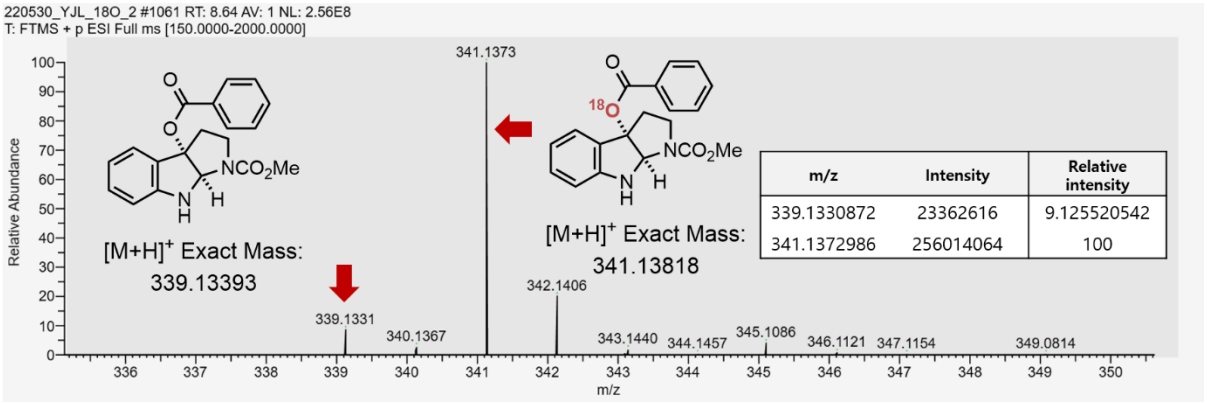
Methyl 3a-(benzoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-A)



Isotopic simulation of positive ion mode



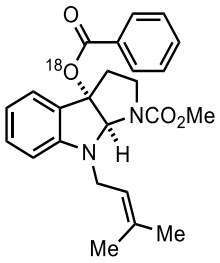
HRMS result of compound **^{18}O-2-A**



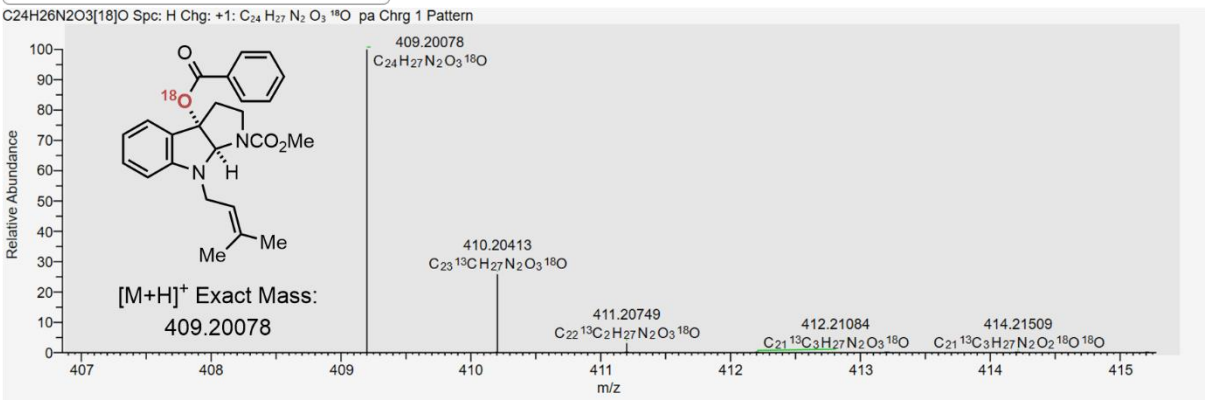
m/z	Intensity	Relative intensity
339.1330872	23362616	9.125520542
341.1372986	256014064	100

^{18}O enrichment: 91.6%

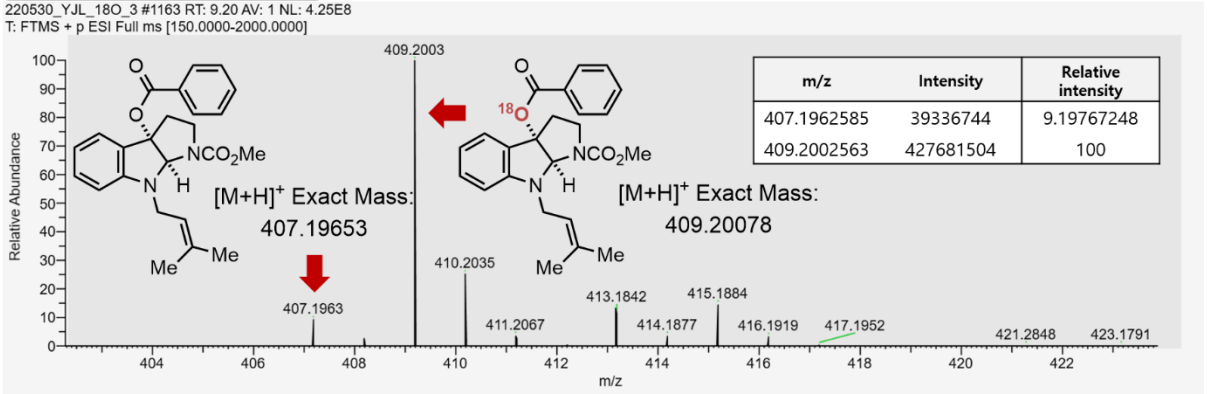
Methyl 3a-(benzoyloxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-A)



Isotopic simulation of positive ion mode



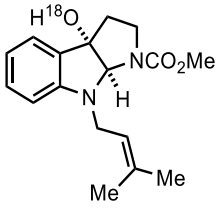
HRMS result of compound **^{18}O-3-A**



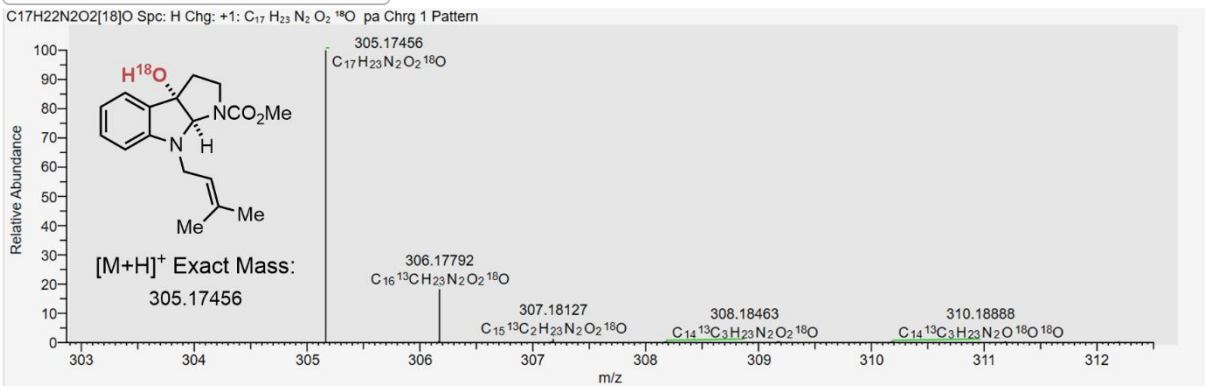
m/z	Intensity	Relative intensity
407.1962585	39336744	9.19767248
409.2002563	427681504	100

^{18}O enrichment: 91.6%

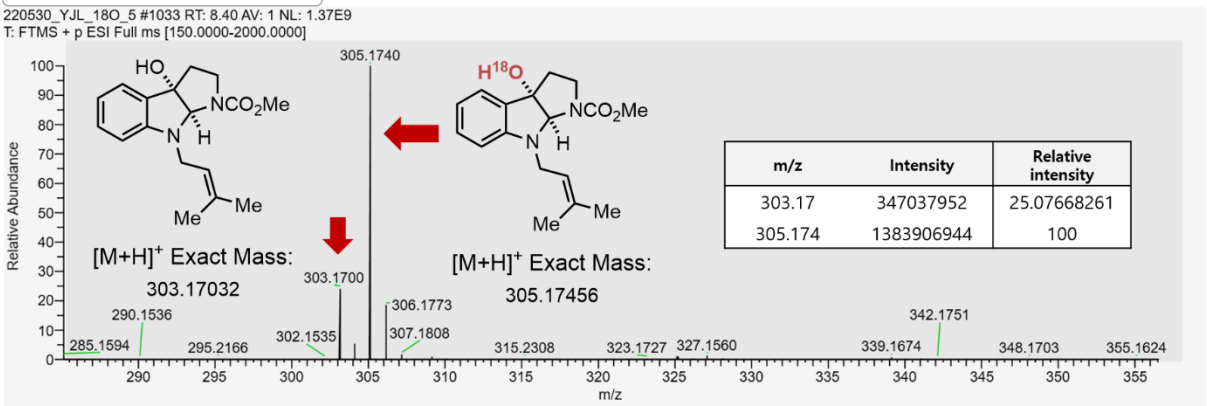
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-A)



Isotopic simulation of positive ion mode



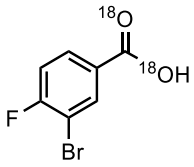
HRMS result of compound **^{18}O-4-A**



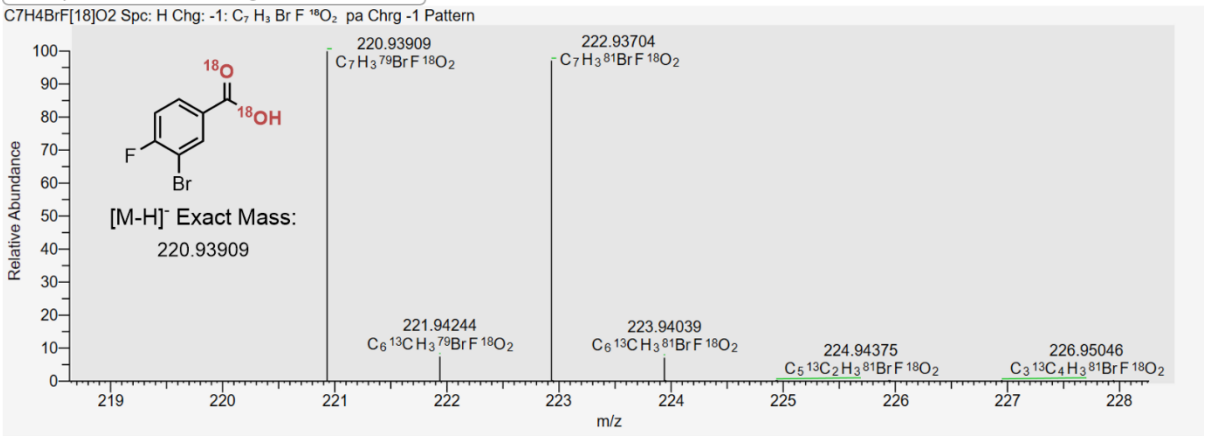
m/z	Intensity	Relative intensity
303.17	347037952	25.07668261
305.174	1383906944	100

^{18}O enrichment: 80.0%

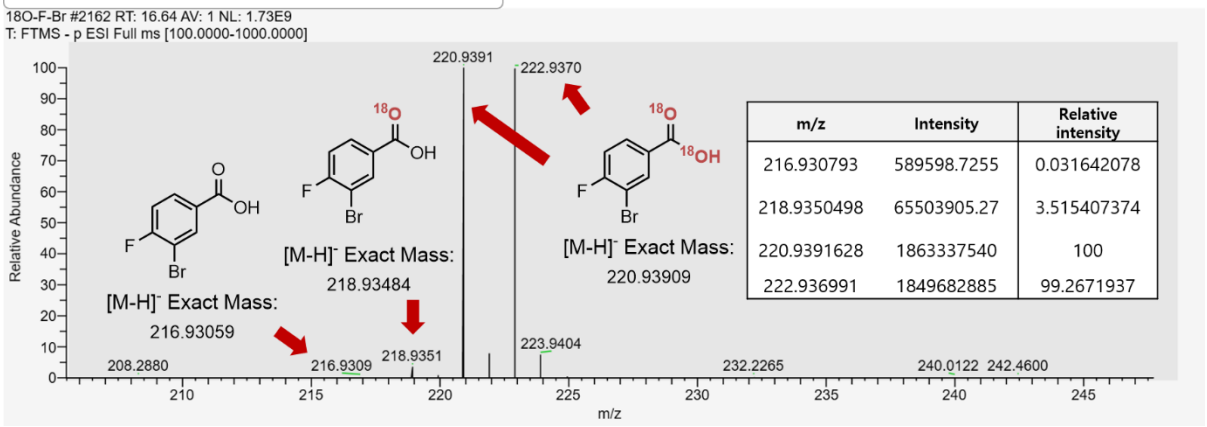
^{18}O-3-Bromo-4-fluorobenzoic acid



Isotopic simulation of negative ion mode

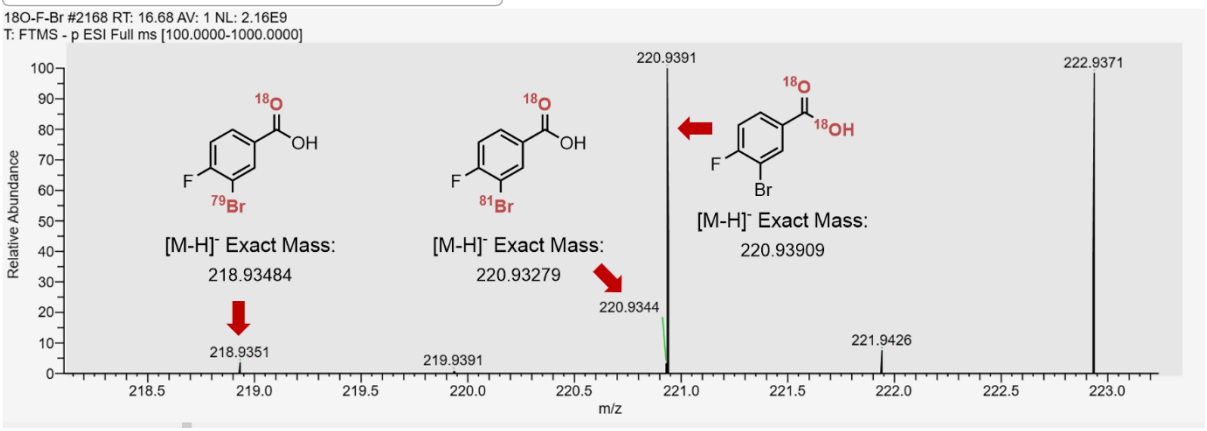


HRMS result of **^{18}O-3-bromo-4-fluorobenzoic acid**

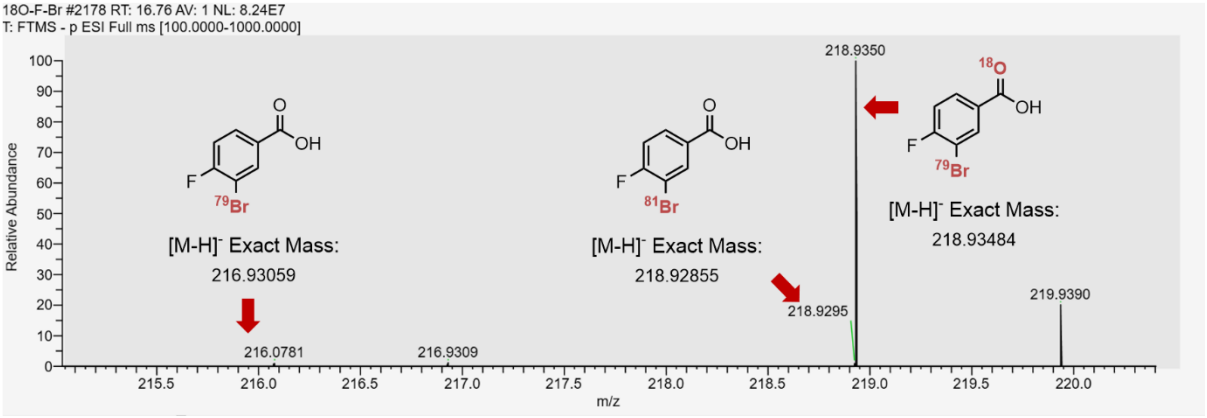


m/z	Intensity	Relative intensity
216.930793	589598.7255	0.031642078
218.9350498	65503905.27	3.515407374
220.9391628	1863337540	100
222.936991	1849682885	99.2671937

HRMS result of ^{18}**O-3-bromo-4-fluorobenzoic acid-2**

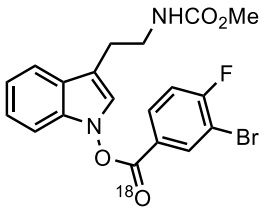


HRMS result of ^{18}**O-3-bromo-4-fluorobenzoic acid-3**

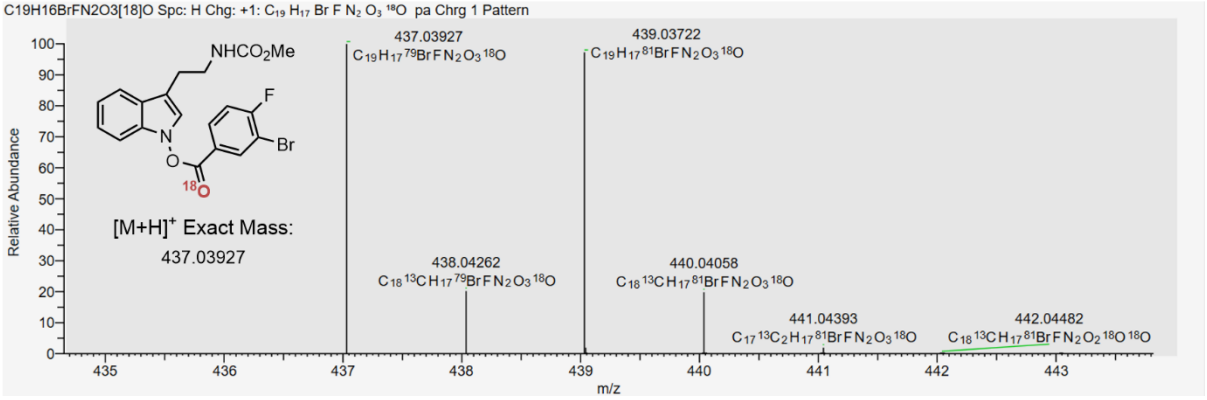


No overlap of isotopes (*i.e.* $C_7H_4{}^{\mathbf{81}}\mathbf{Br}FO_2$ and $C_7H_4{}^{79}BrFO^{\mathbf{18}}\mathbf{O}$) on HRMS was observed.

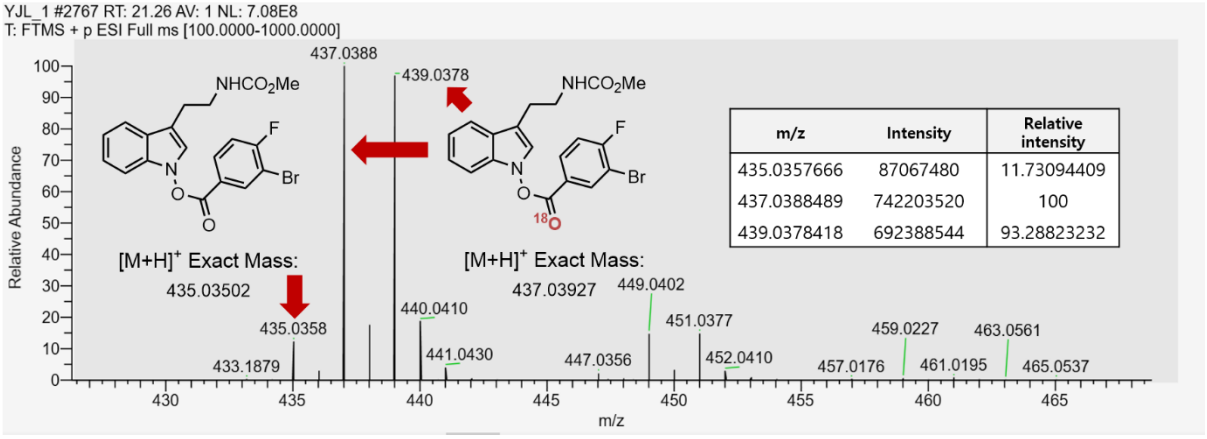
3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl 3-bromo-4-fluorobenzoate (^{18}O-1-B)



Isotopic simulation of positive ion mode



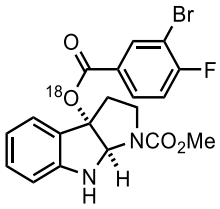
HRMS result of compound **^{18}O-1-B**



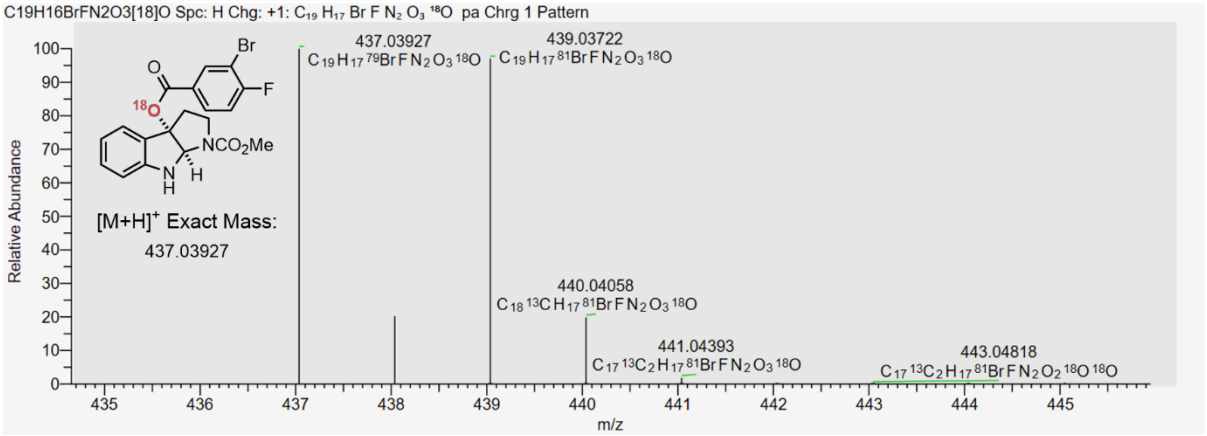
m/z	Intensity	Relative intensity
435.0357666	87067480	11.73094409
437.0388489	742203520	100
439.0378418	692388544	93.28823232

^{18}O enrichment: 89.5%

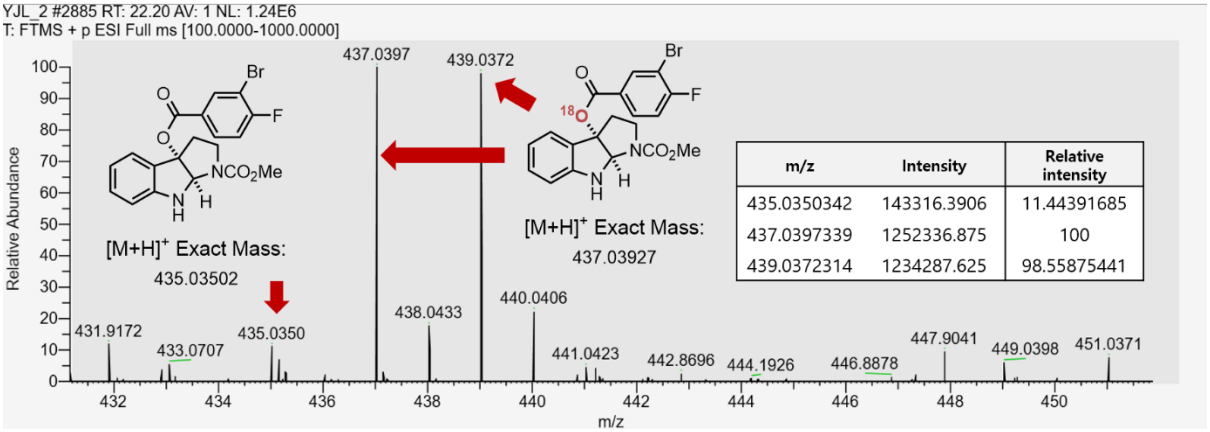
Methyl 3a-((3-bromo-4-fluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-B)



Isotopic simulation of positive ion mode



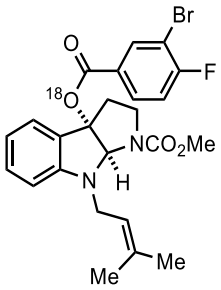
HRMS result of compound **^{18}O-2-B**



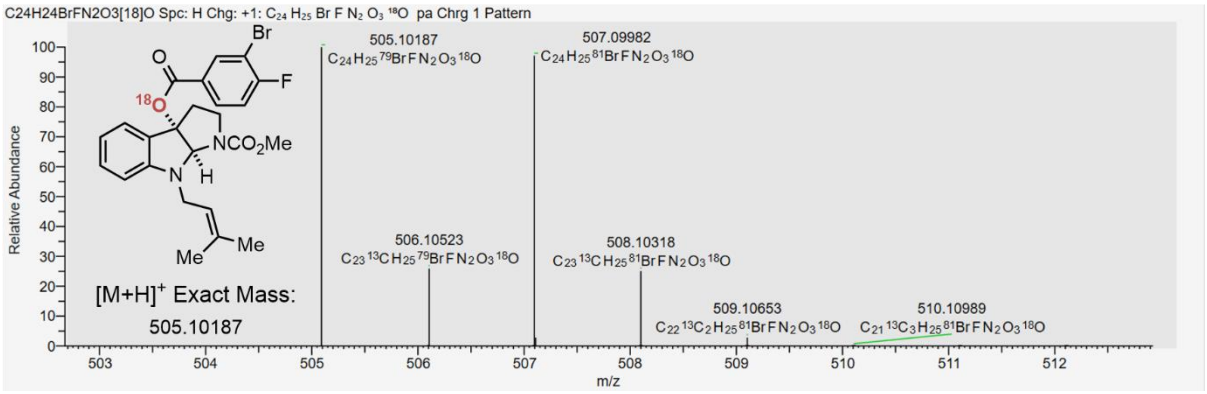
m/z	Intensity	Relative intensity
435.0350342	143316.3906	11.44391685
437.0397339	1252336.875	100
439.0372314	1234287.625	98.55875441

^{18}O enrichment: 89.7%

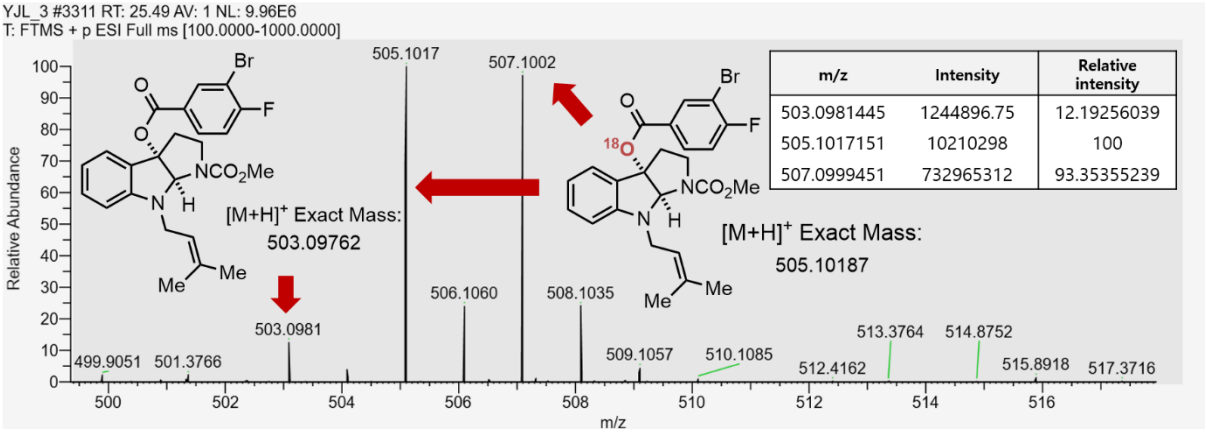
Methyl 3a-((3-bromo-4-fluorobenzoyl)oxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-B)



Isotopic simulation of positive ion mode



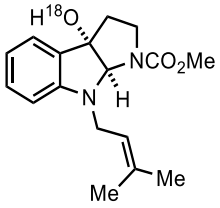
HRMS result of compound **^{18}O-3-B**



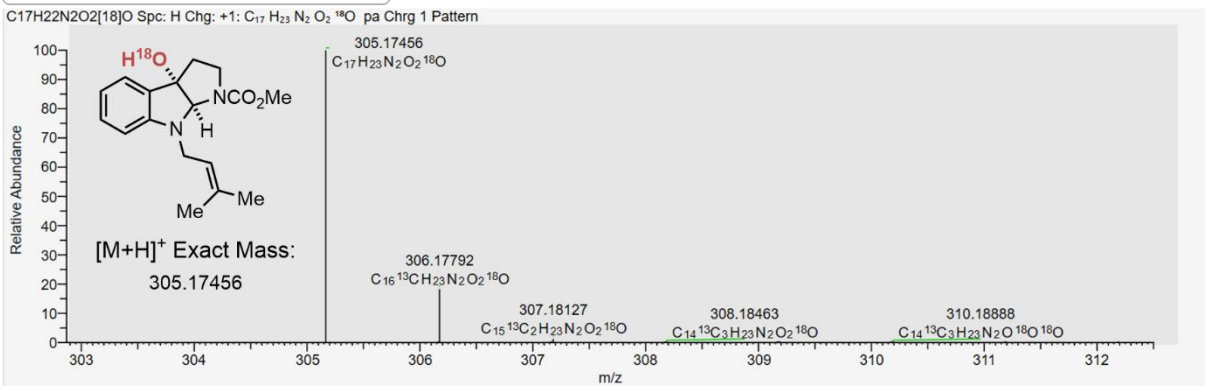
m/z	Intensity	Relative intensity
503.0981445	1244896.75	12.19256039
505.1017151	10210298	100
507.0999451	732965312	93.35355239

^{18}O enrichment: 89.1%

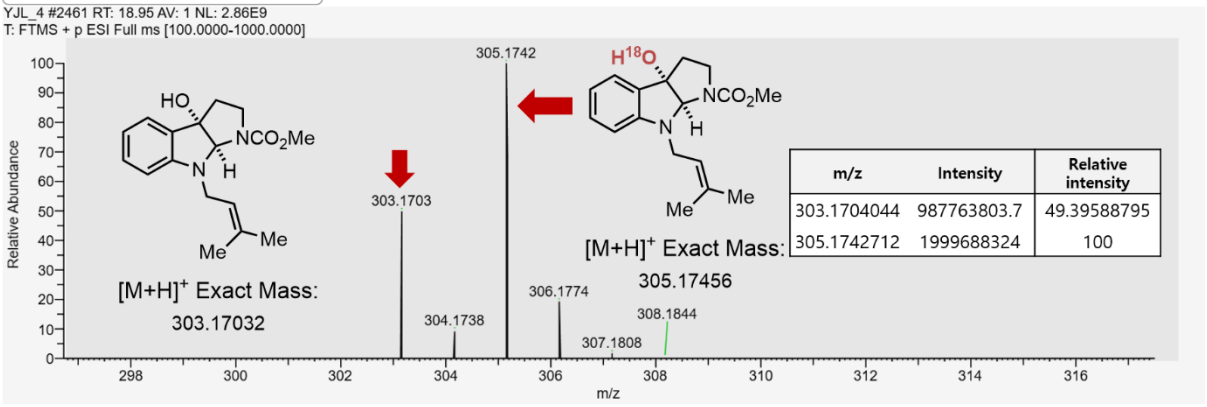
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-B)



Isotopic simulation of positive ion mode



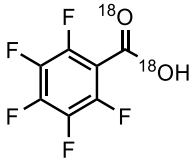
HRMS result of compound **^{18}O-4-B**



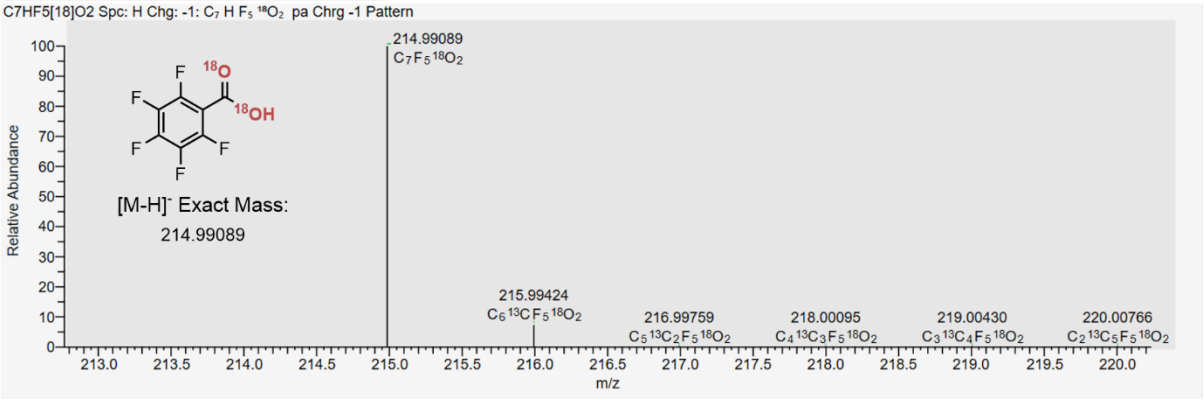
m/z	Intensity	Relative intensity
303.1704044	987763803.7	49.39588795
305.1742712	1999688324	100

^{18}O enrichment: 66.9%

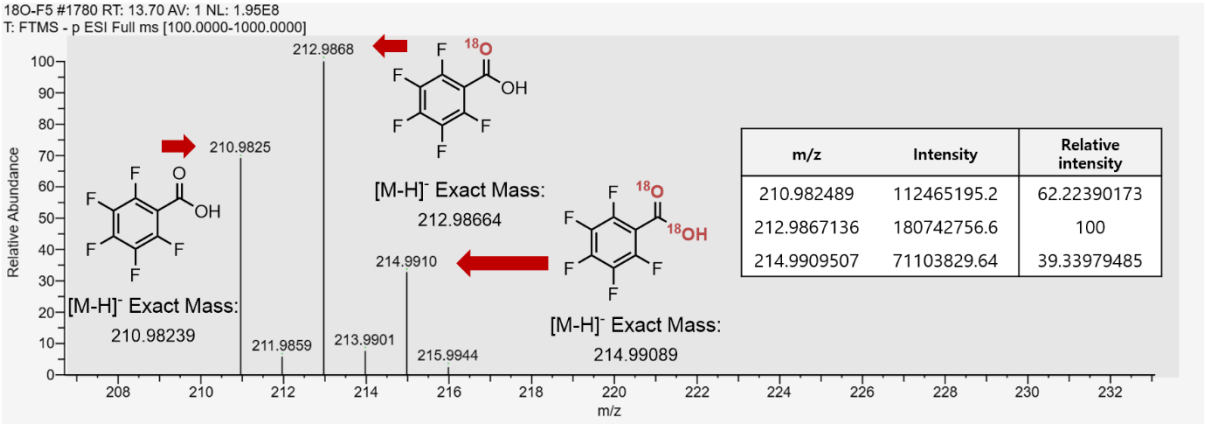
^{18}O-2,3,4,5,6-Pentafluorobenzoic acid



Isotopic simulation of negative ion mode

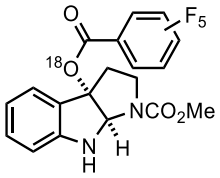


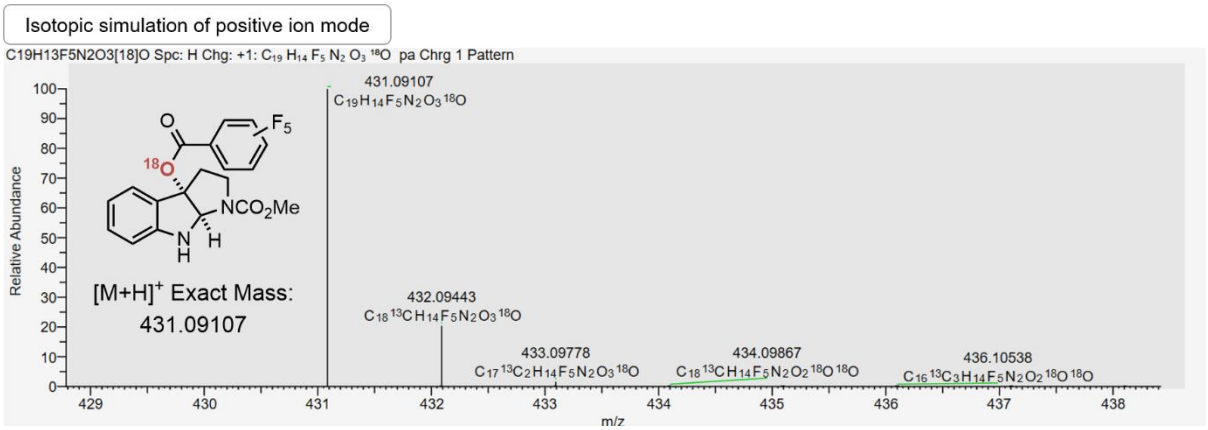
HRMS result of **^{18}O-pentafluorobenzoic acid**

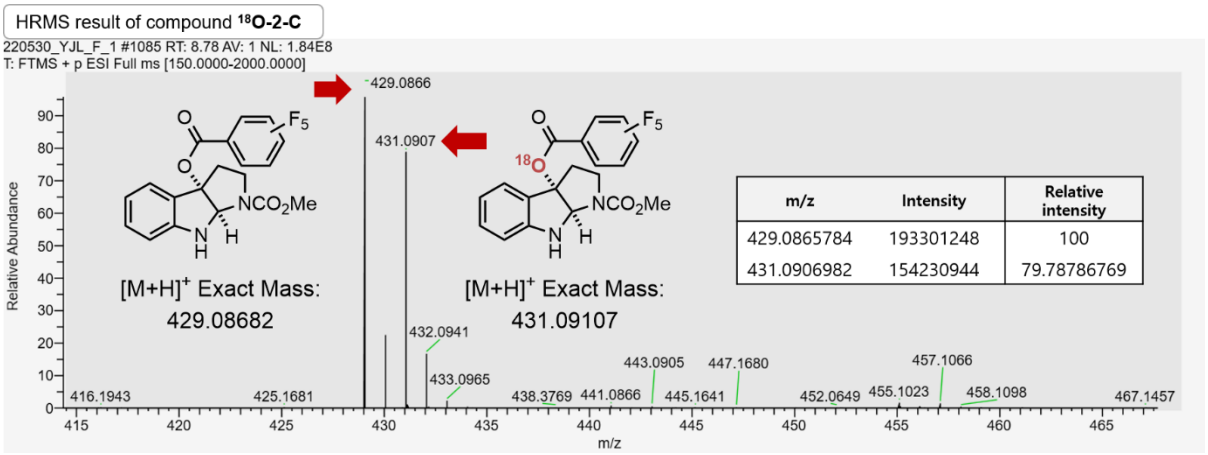


m/z	Intensity	Relative intensity
210.982489	112465195.2	62.22390173
212.9867136	180742756.6	100
214.9909507	71103829.64	39.33979485

Methyl 3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-C)

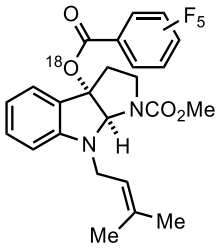




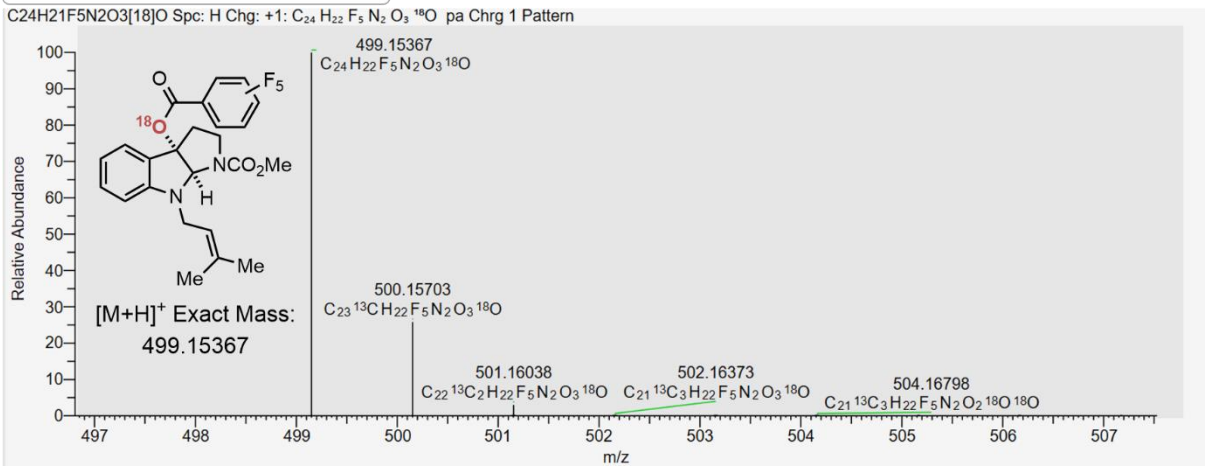


^{18}O enrichment: 44.4%

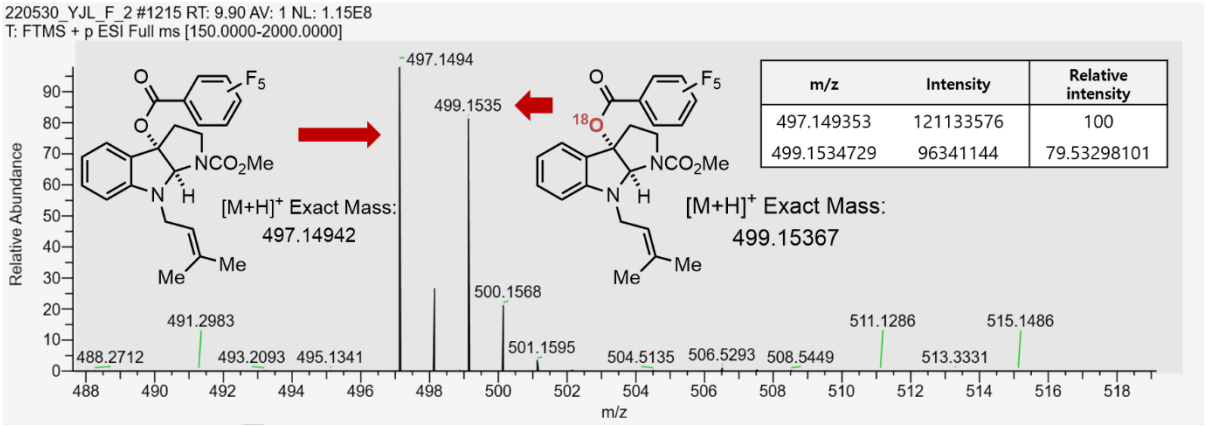
Methyl 8-(3-methylbut-2-en-1-yl)-3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-C)



Isotopic simulation of positive ion mode



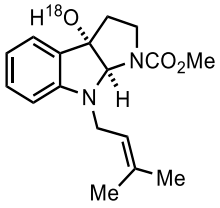
HRMS result of compound **^{18}O-3-C**



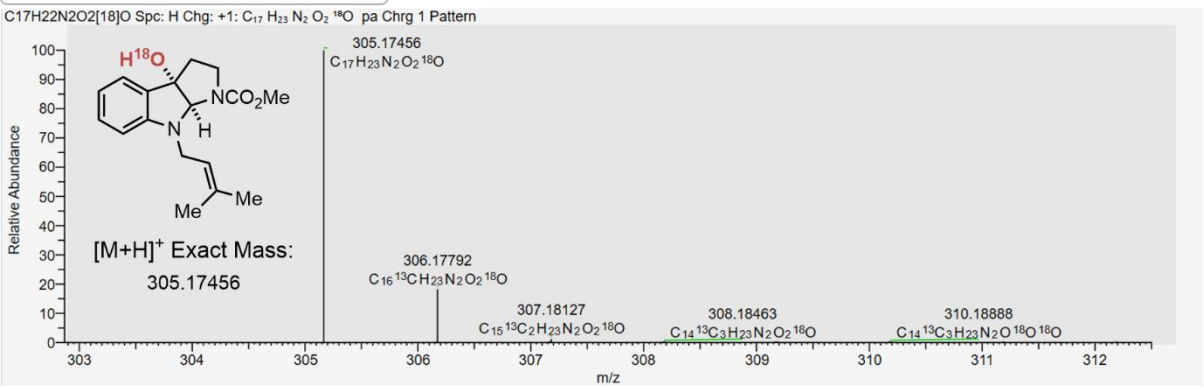
m/z	Intensity	Relative intensity
497.149353	121133576	100
499.1534729	96341144	79.53298101

^{18}O enrichment: 44.3%

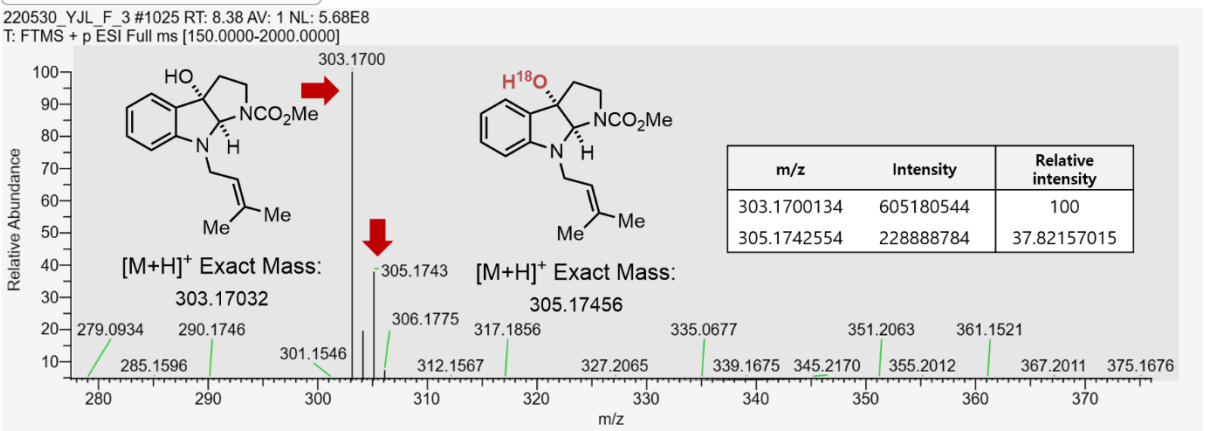
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-C)



Isotopic simulation of positive ion mode



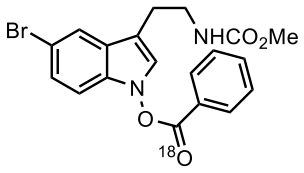
HRMS result of compound **^{18}O-4-C**

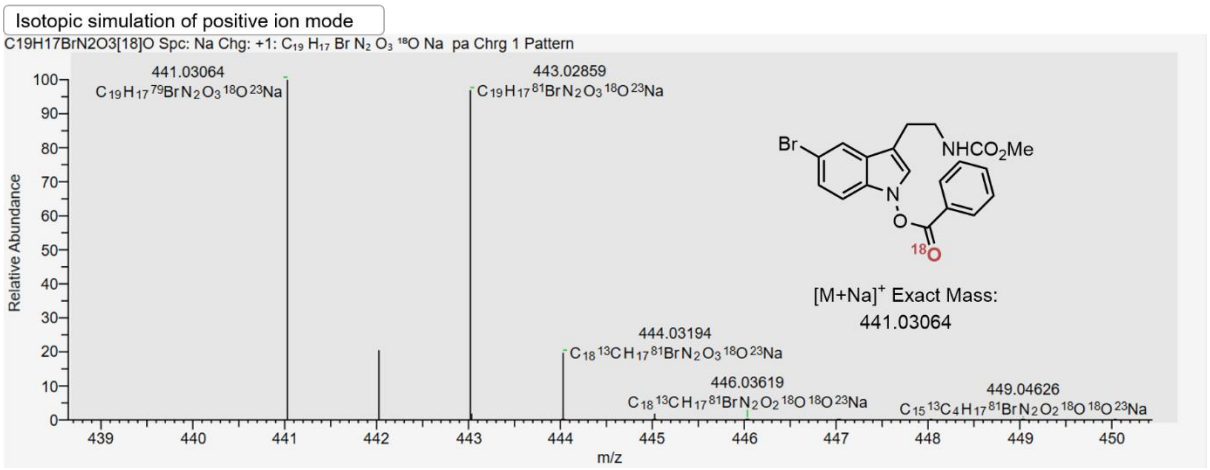


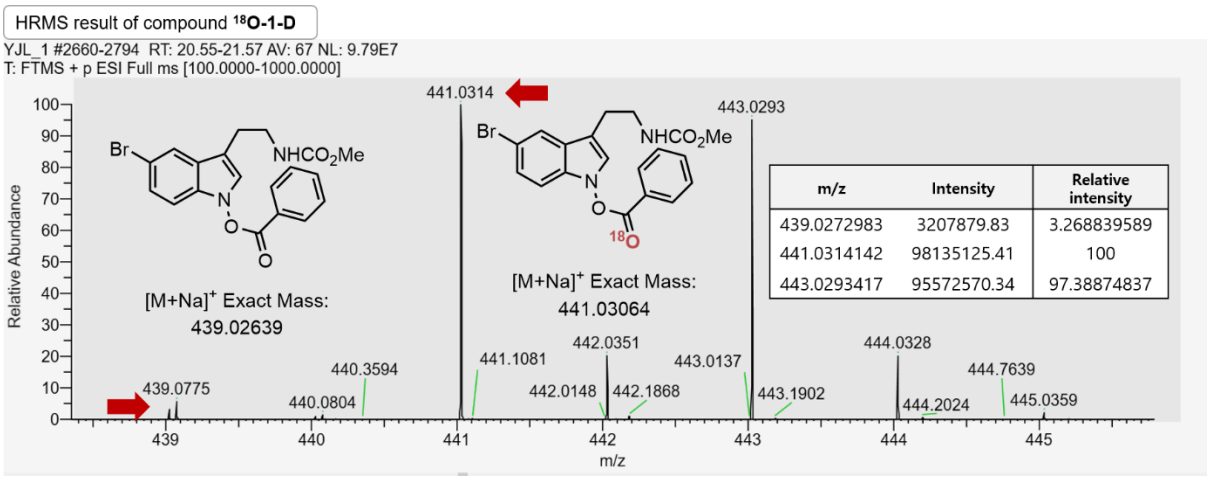
m/z	Intensity	Relative intensity
303.1700134	605180544	100
305.1742554	228888784	37.82157015

^{18}O enrichment: 27.4%

5-Bromo-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (^{18}O-1-D)



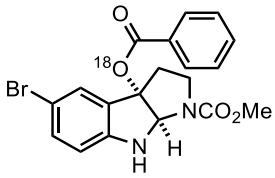


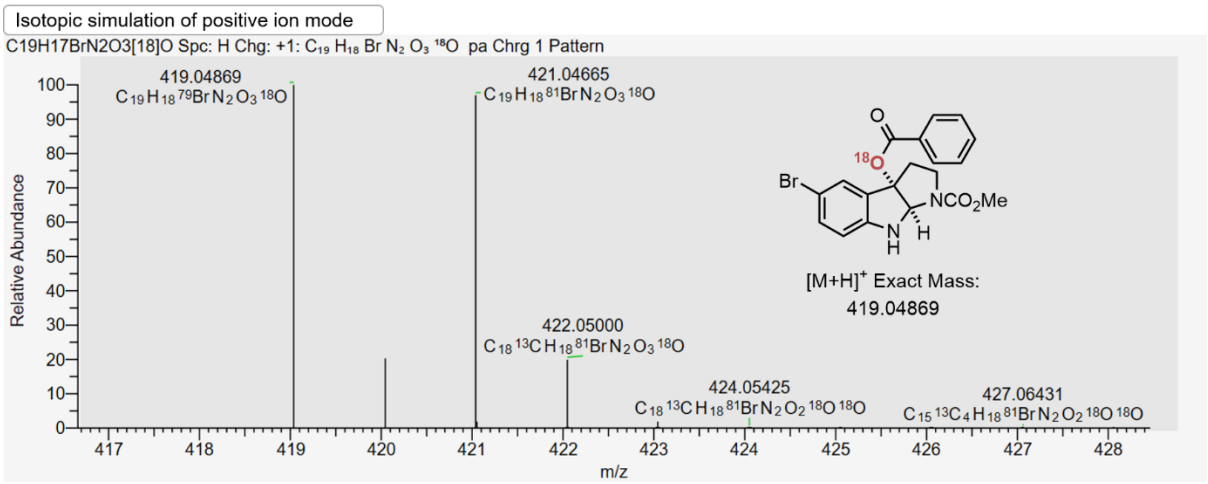


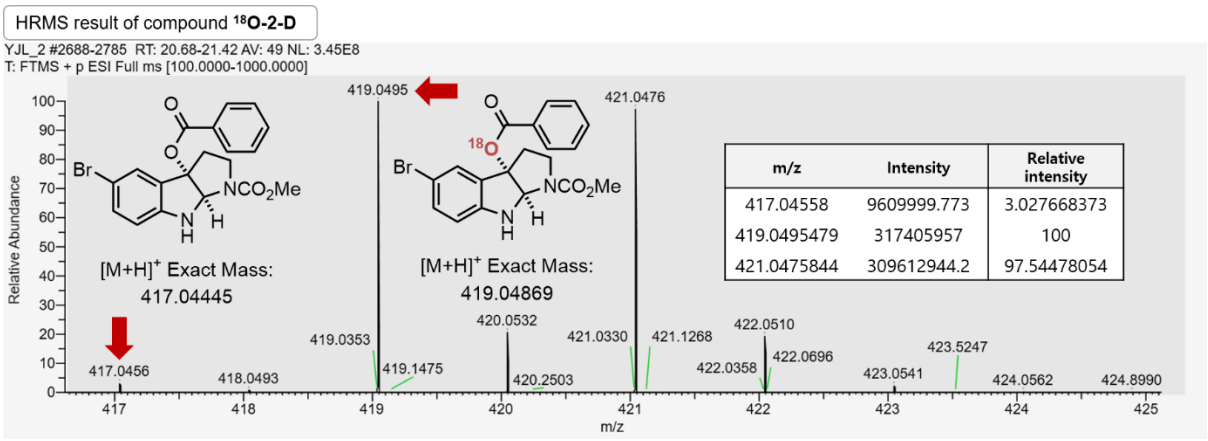
m/z	Intensity	Relative intensity
439.0272983	3207879.83	3.268839589
441.0314142	98135125.41	100
443.0293417	95572570.34	97.38874837

^{18}O enrichment: 96.8%

Methyl 3a-(benzoyloxy)-5-bromo-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-D)

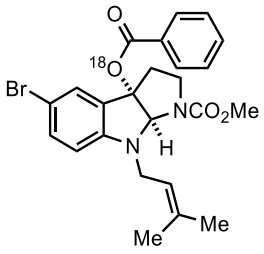


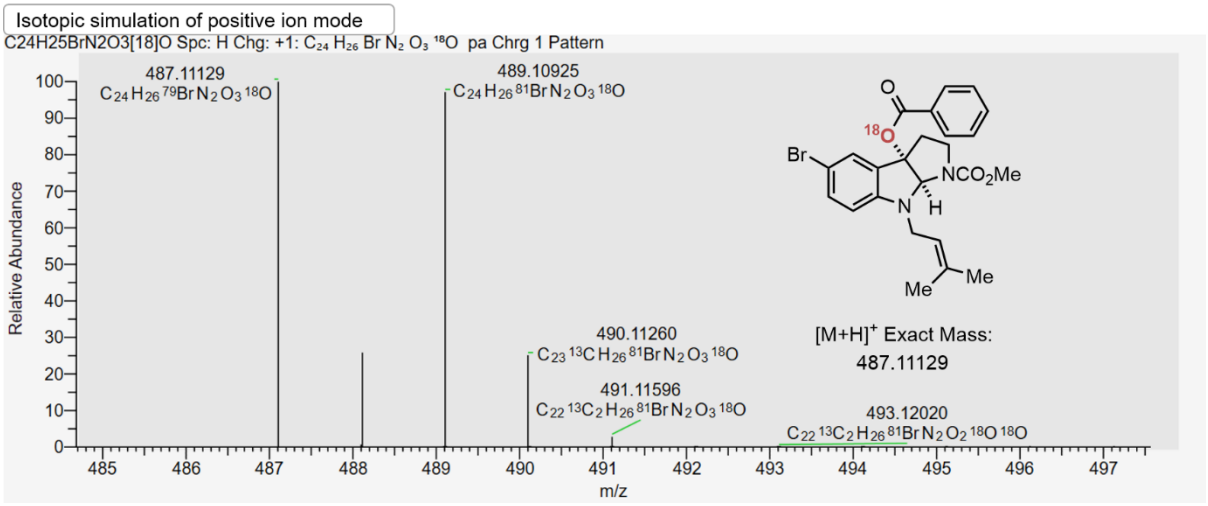


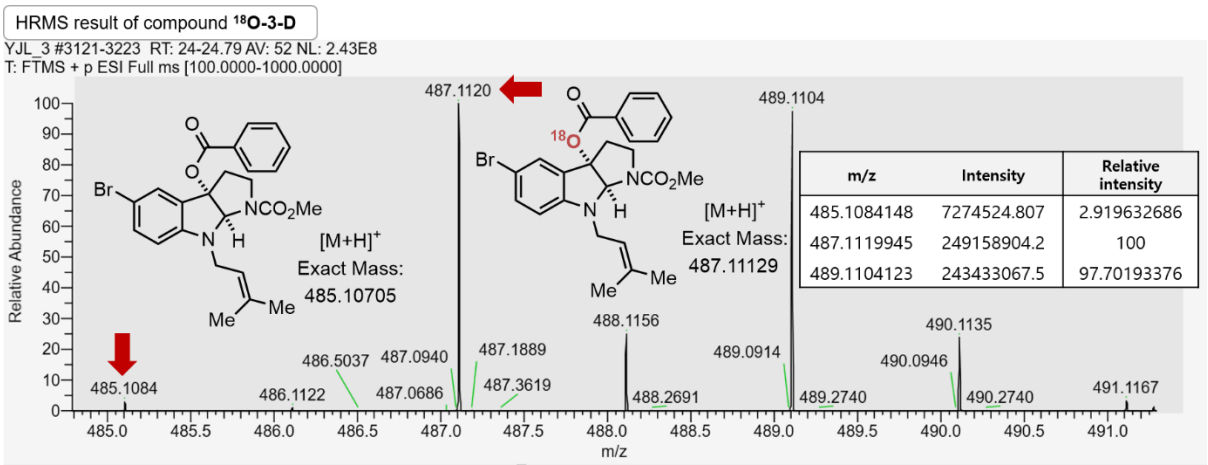


^{18}O enrichment: 97.1%

Methyl 3a-(benzoyloxy)-5-bromo-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-D)



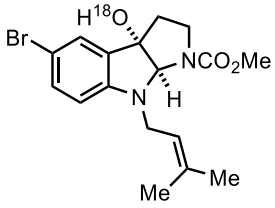


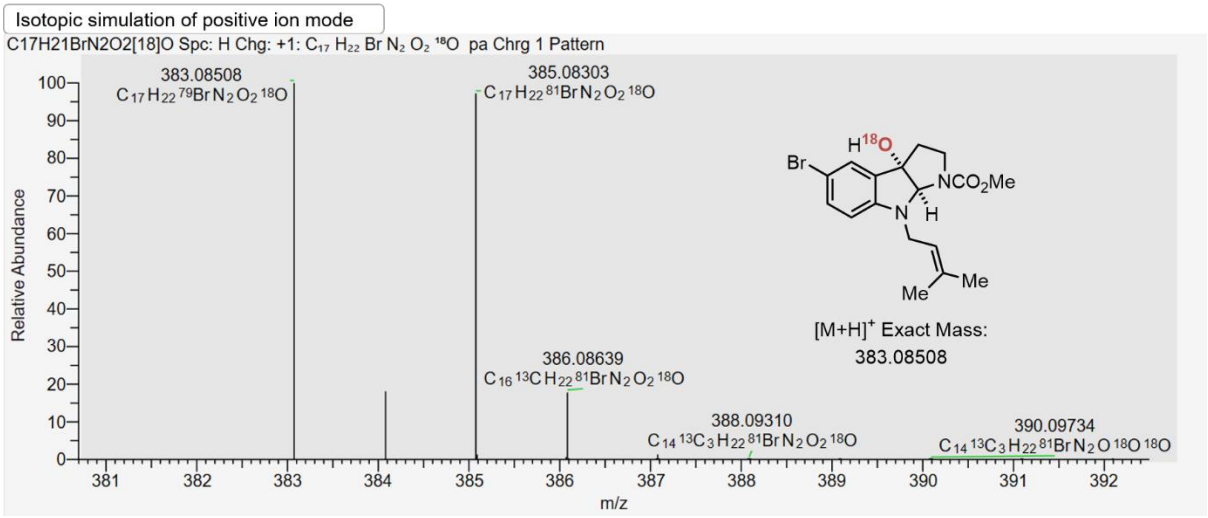


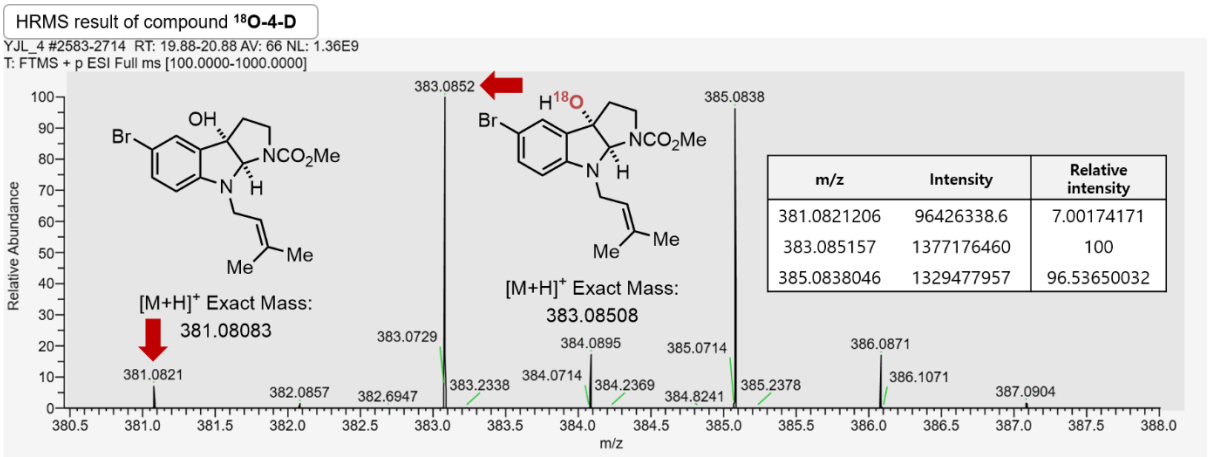
m/z	Intensity	Relative intensity
485.1084148	7274524.807	2.919632686
487.1119945	249158904.2	100
489.1104123	243433067.5	97.70193376

^{18}O enrichment: 97.2%

Methyl 5-bromo-3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-D)

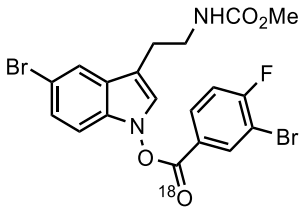




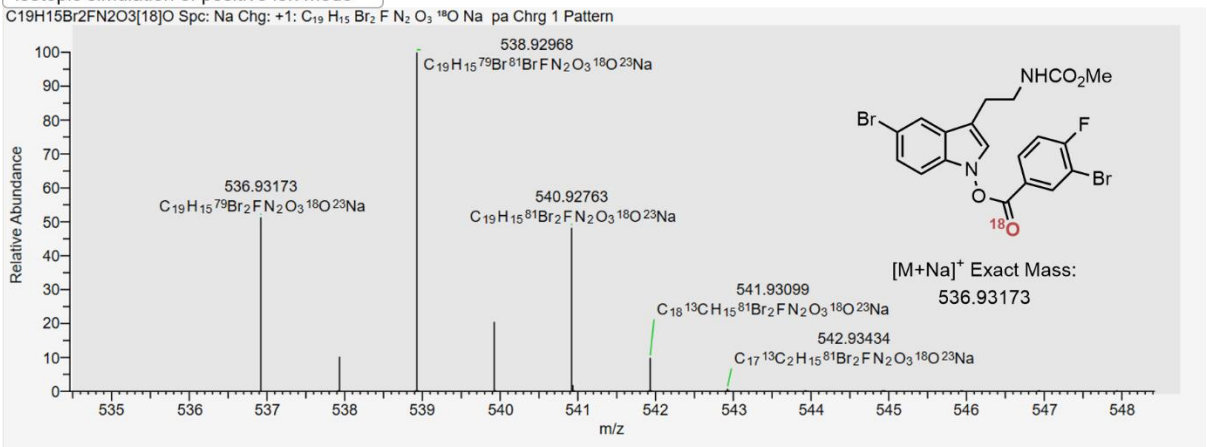


^{18}O enrichment: 93.5%

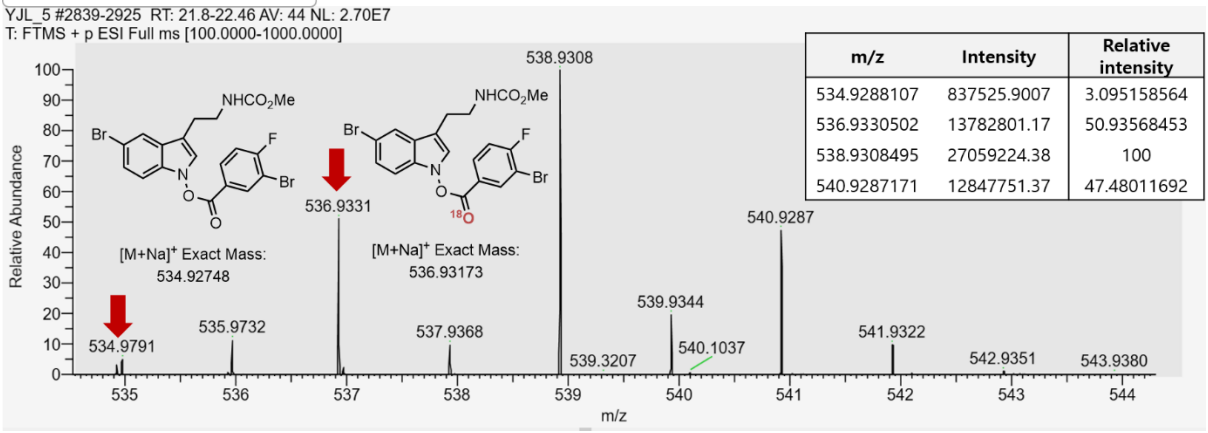
5-Bromo-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indol-1-yl 3-bromo-4-fluorobenzoate (^{18}O-1-E)



Isotopic simulation of positive ion mode



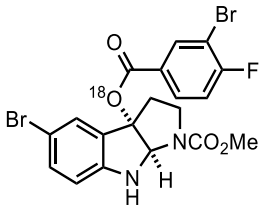
HRMS result of compound **^{18}O-1-E**

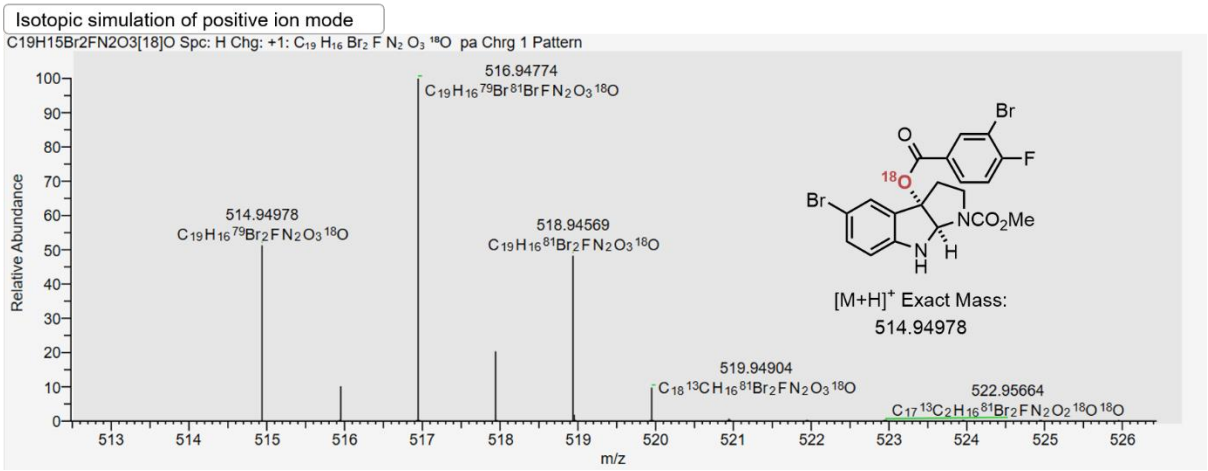


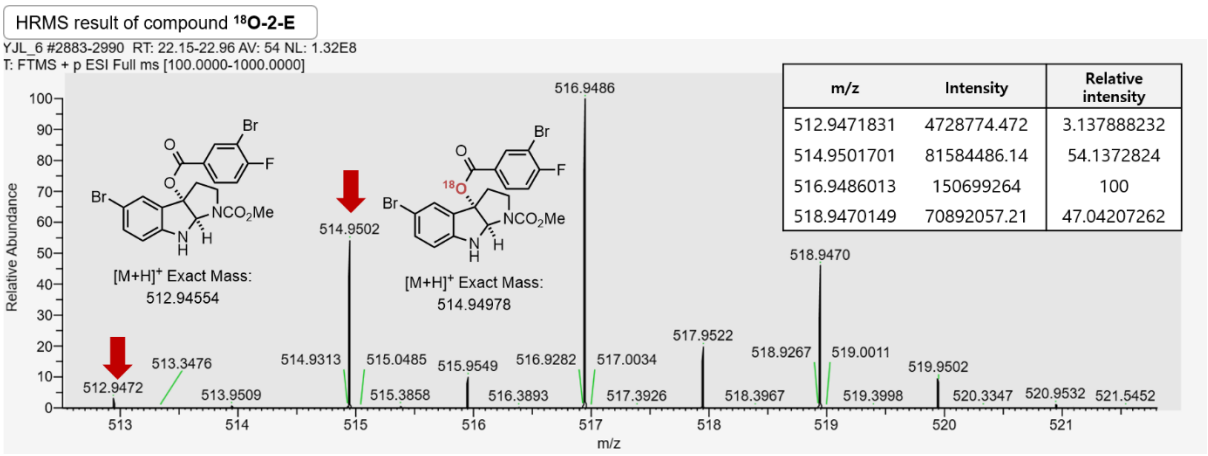
m/z	Intensity	Relative intensity
534.9288107	837525.9007	3.095158564
536.9330502	13782801.17	50.93568453
538.9308495	27059224.38	100
540.9287171	12847751.37	47.48011692

^{18}O enrichment: 94.3%

Methyl 5-bromo-3a-((3-bromo-4-fluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-2-E)



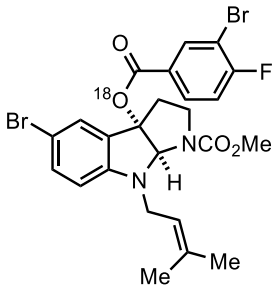


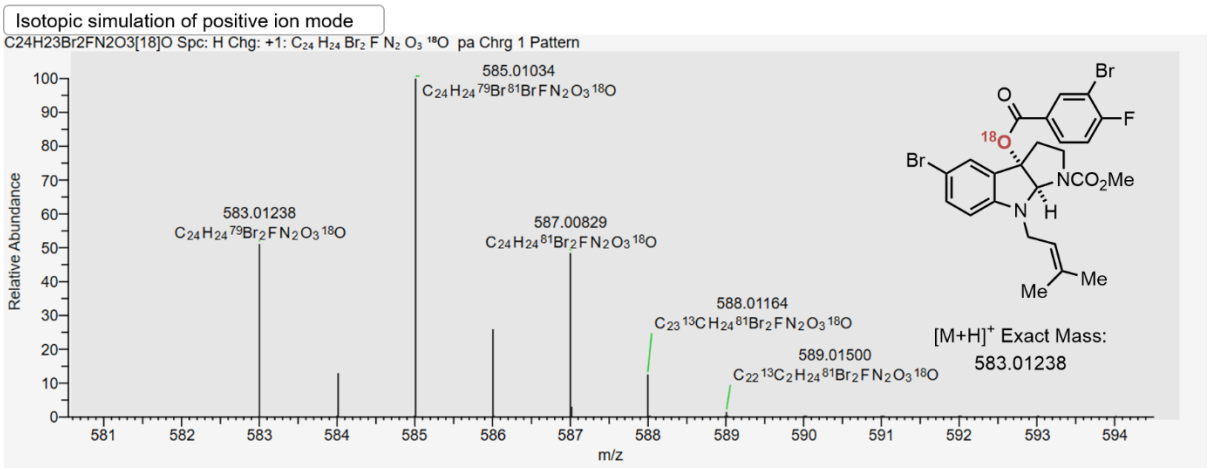


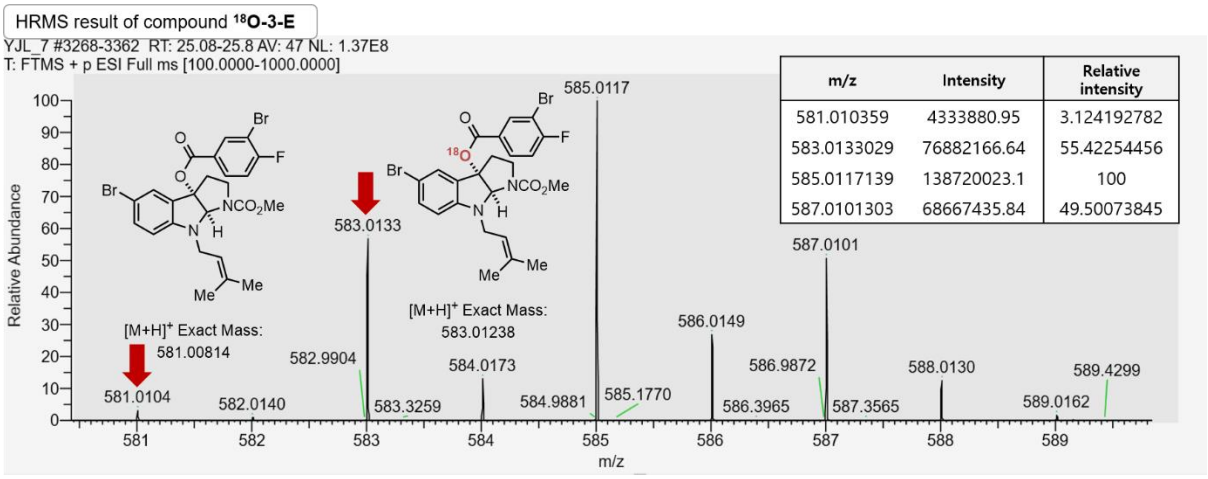
m/z	Intensity	Relative intensity
512.9471831	4728774.472	3.137888232
514.9501701	81584486.14	54.1372824
516.9486013	150699264	100
518.9470149	70892057.21	47.04207262

^{18}O enrichment: 94.5%

Methyl 5-bromo-3a-((3-bromo-4-fluorobenzoyl)oxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-3-E)



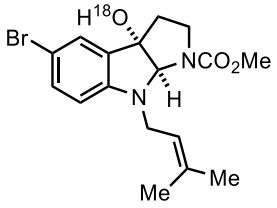


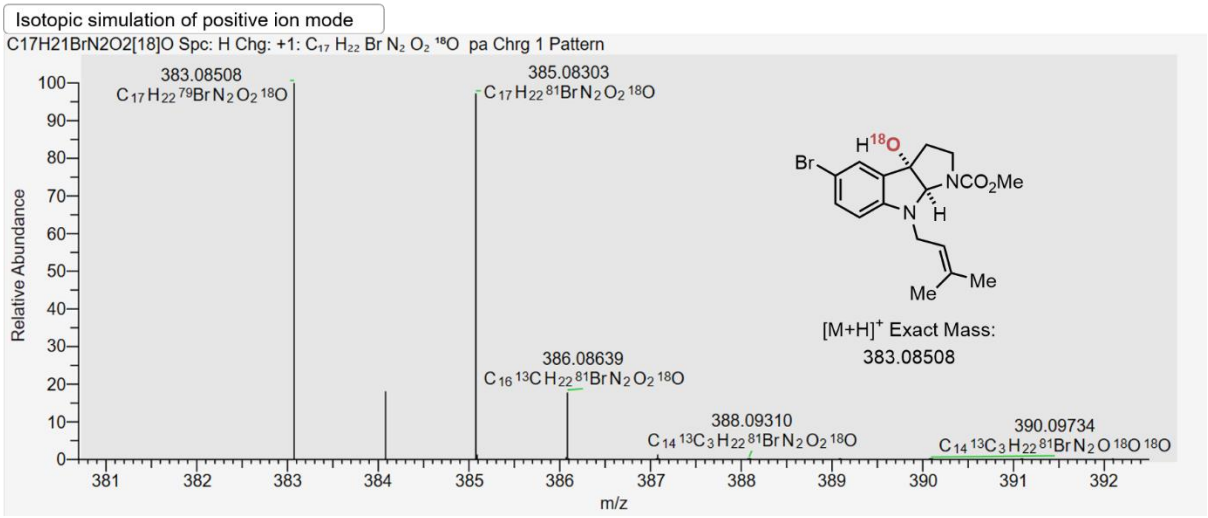


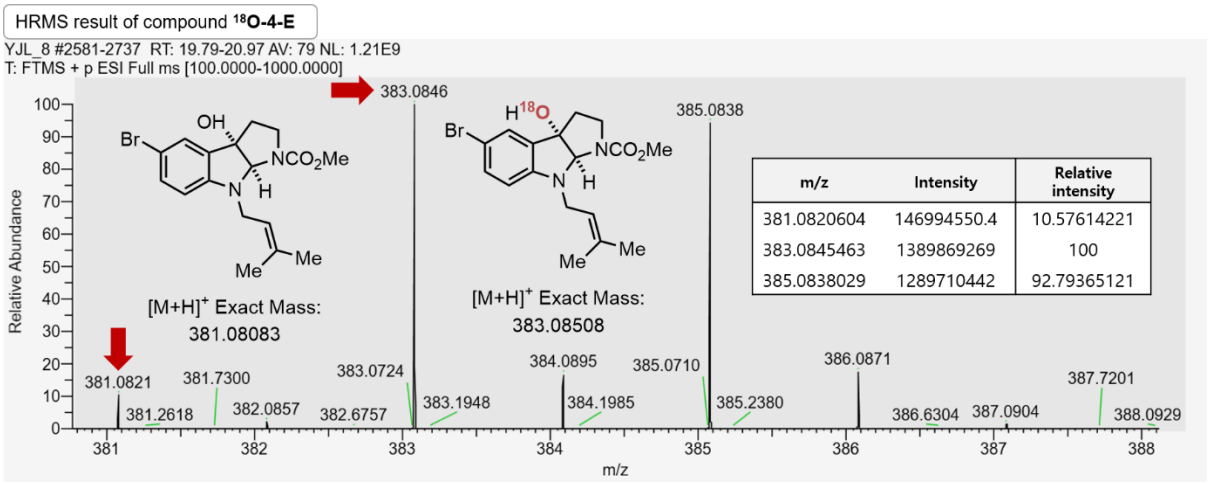
m/z	Intensity	Relative intensity
581.010359	4333880.95	3.124192782
583.0133029	76882166.64	55.42254456
585.0117139	138720023.1	100
587.0101303	68667435.84	49.50073845

^{18}O enrichment: 94.7%

Methyl 5-bromo-3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (^{18}O-4-E)





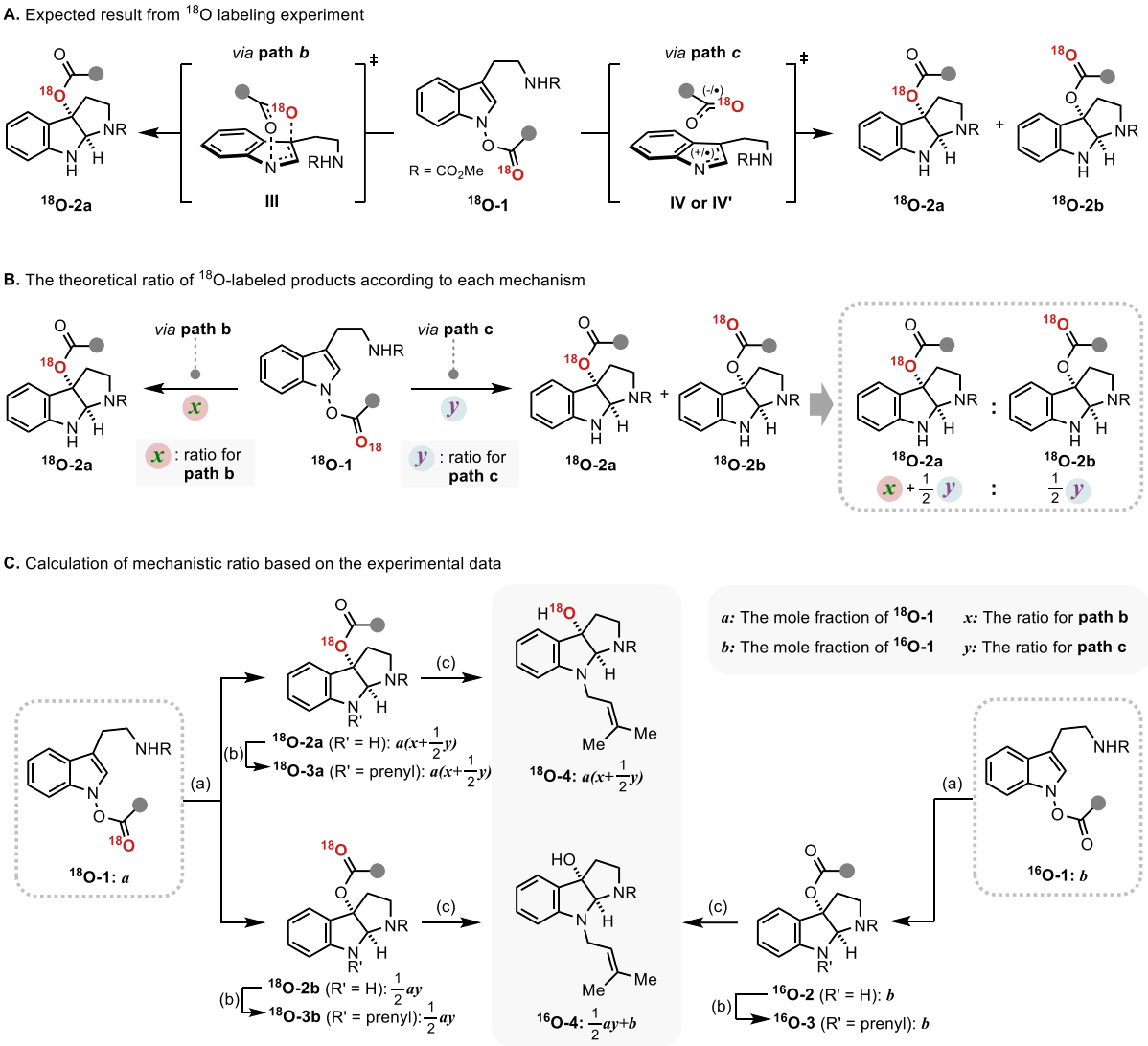


^{18}O enrichment: 90.4%

3.2.3. Quantitative Analysis of ^{18}O-Labeling Experiment Results (Figures 4 and 5)

3.2.3.1. Dependence of the electronic properties (Figure 4)

Assuming **path b** and **path c** are primarily operating for the **IHT** process, the relative contribution of each pathway could be determined. The formation of **^{18}O-4** is attributed to the action of **path b** from **^{18}O-1** in total, and half the participation of **path c** from the identical starting material. The other half of the involvement of **path c** from **^{18}O-1**, along with the rearrangement from ^{18}O-free starting material, **^{16}O-1**, generates the unlabeled oxygenation product **^{16}O-4**.



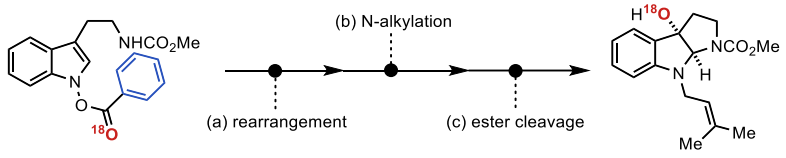
Conditions:(a) For **^{18}O-1-A**: toluene, 90 °C, 16 h, for **^{18}O-1-B**: toluene, 70 °C, 8 h, for **^{18}O-1-C**: CH_2Cl_2, 0 °C, 2 h; (b) For **^{18}O-2-A, ^{18}O-2-B**: 1-bromo-3-methyl-2-butene (1.5 equiv), K_2CO_3 (3.0 equiv), acetone, 23 °C, 16 h, for **^{18}O-2-C**: 1-bromo-3-methyl-2-butene (3.0 equiv), K_2CO_3 (6.0 equiv), acetone, 23 °C, 4 d; (c) KOH (1.5 equiv), EtOH:H_2O = 5 :1, 60 °C, 3 h

Figure S3. Schematic explanation for the calculation of the ratio of each pathway.

The relative contribution of each pathway for the formation of the IHT product was determined based on the following premises. **path b** will exclusively produce **^{18}O-2a** as a sole product while **path c** will form **^{18}O-2a** and **^{18}O-2b** in a 1:1 ratio, respectively.

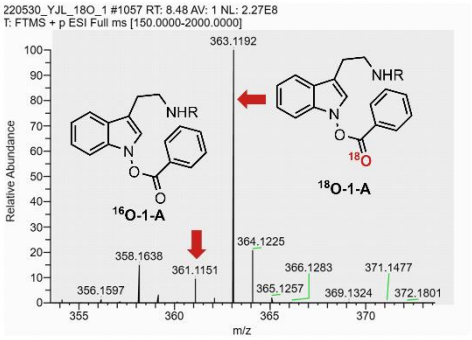
The mole fraction of **^{18}O-1** is denoted as *a*, and since the ^{18}O enrichment is not 100%, the mole fraction of naturally existing **^{16}O-1** is defined as *b*. Also, the relative contribution of **path b** for the formation of the product is denoted as *x*, and the relative contribution of **path c** for the formation of the product is defined as *y*. The ratio between **^{18}O-4** and **^{16}O-4** is expressed as $a(x+\frac{1}{2}y)$: $\frac{1}{2}ay+b$ (Figure S3). Detailed calculation process is attached below.

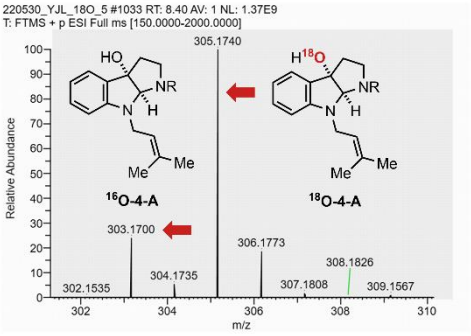
(1) **IHT** reaction with benzoyl substituent



^{18}O-1-A
92% [^{18}O]

^{18}O-4-A
80% [^{18}O]





^{18}O-1-A:^{16}O-1-A = *a : b = 100 : 9.3*

^{18}O-4-A:^{16}O-4-A = $a(x+\frac{1}{2}y) : \frac{1}{2}ay+b = 100 : 25.1$

The system of equations is established by the two proportional expressions:

$$\begin{cases} a:b = 100:9.3 & (1) \\ a(x+\frac{1}{2}y):\frac{1}{2}ay+b = 100:25.1 & (2) \end{cases}$$

From equation 1, ***b*** can be expressed as:

$$b = \frac{93}{1000}a \qquad (3)$$

Insertion of the equation 3 into equation 2 gives equation 4:

$$\mathrm{a}(x+\frac{1}{2}y):\frac{1}{2}ay+\frac{93}{1000}a = 100:25.1 \qquad (4)$$

$$\therefore x+\frac{1}{2}y:\frac{1}{2}y+\frac{93}{1000} = 100:25.1$$

$$\therefore 50y+9.3 = 25.1x+\frac{251}{20}y$$

$$\therefore 25.1x-\frac{749}{20}y = 9.3 \qquad (5)$$

Since ***y*** is defined in terms of 1–***x***, the equation 5 can be re-written as:

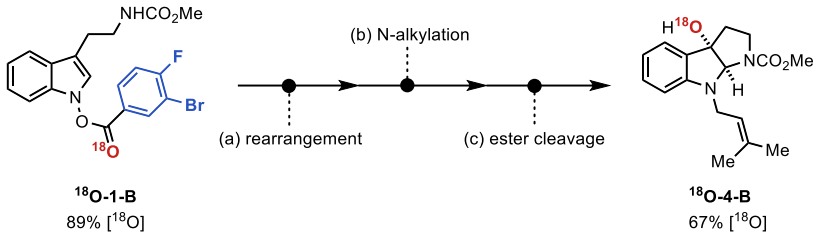
$$25.1x-\frac{749}{20}(1-x) = 9.3$$

$$\therefore 62.6x = 46.8$$

$$\therefore x = 0.75 \qquad (6)$$

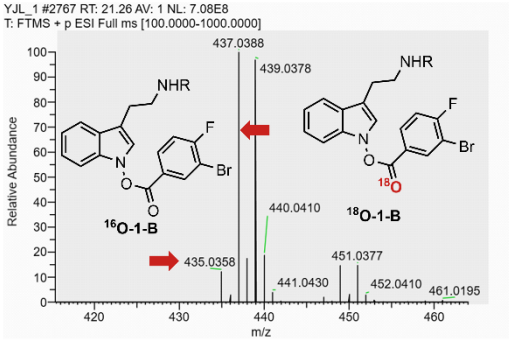
$$\therefore y = 1-x = 0.25 \qquad (7)$$

(2) **IHT** reaction with 3-bromo-4-fluorobenzoyl substituent

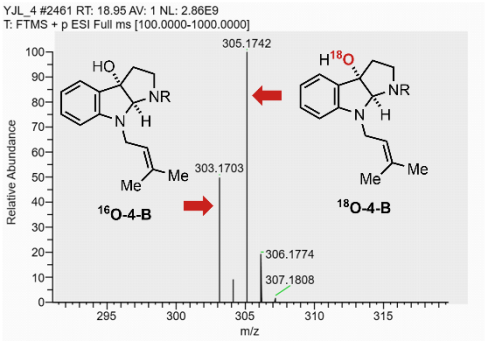


^{18}O-1-B
89% [^{18}O]

^{18}O-4-B
67% [^{18}O]



^{18}O-1-B:^{16}O-1-B = $a : b = 100 : 11.7$



^{18}O-4-B:^{16}O-4-B = $a(x+\frac{1}{2}y) : \frac{1}{2}ay+b = 100 : 49.4$

The system of equations is established by the two proportional expressions:

$$\begin{cases} a : b = 100 : 11.7 & (1) \\ a(x+\frac{1}{2}y) : \frac{1}{2}ay + b = 100 : 49.4 & (2) \end{cases}$$

From equation 1, ***b*** can be expressed as:

$$b = \frac{117}{1000}a \qquad (3)$$

Insertion of the equation 3 into equation 2 gives equation 4:

$$\mathrm{a}(x+\frac{1}{2}y) : \frac{1}{2}ay + \frac{117}{1000}a = 100 : 49.4 \qquad (4)$$

$$\therefore x+\frac{1}{2}y : \frac{1}{2}y + \frac{117}{1000} = 100 : 49.4$$

$$\therefore 50y + 11.7 = 49.4x + \frac{494}{20}y$$

$$\therefore 49.4x - \frac{506}{20}y = 11.7 \qquad (5)$$

Since ***y*** is defined in terms of 1–***x***, the equation 5 can be re-written as:

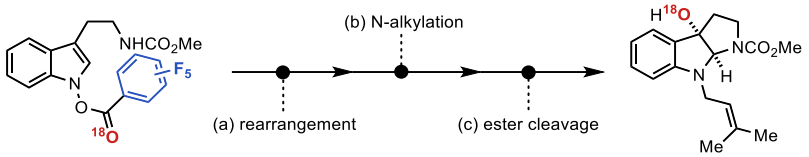
$$49.4x - \frac{506}{20}(1-x) = 11.7$$

$$\therefore 74.7x = 37$$

$$\therefore x = 0.49 \qquad (6)$$

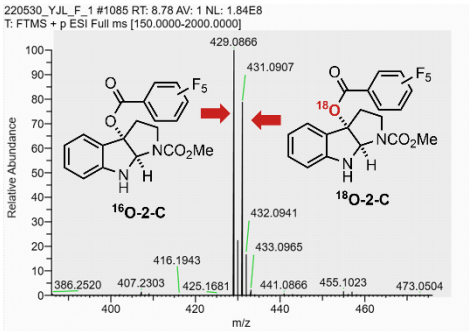
$$\therefore y = 1 - x = 0.51 \qquad (7)$$

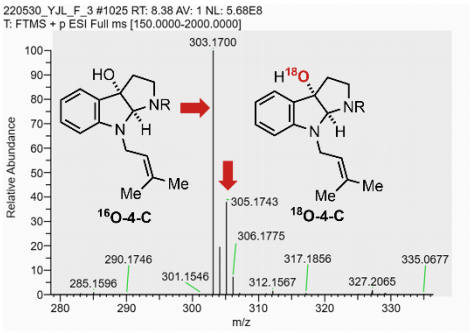
(3) **IHT** reaction with pentafluorobenzoyl substituent



^{18}O-1-C
44% [^{18}O]

^{18}O-4-C
27% [^{18}O]





^{18}O-2-C:^{16}O-2-C = $a : b = 79.8 : 100$

^{18}O-4-C:^{16}O-4-C = $a(x+\frac{1}{2}y) : \frac{1}{2}ay+b = 37.8 : 100$

The system of equations is established by the two proportional expressions:

$$\begin{cases} a : b = 79.8 : 100 & (1) \\ a(x+\frac{1}{2}y) : \frac{1}{2}ay + b = 37.8 : 100 & (2) \end{cases}$$

From equation 1, ***b*** can be expressed as:

$$b = \frac{1000}{798}a \qquad (3)$$

Insertion of the equation 3 into equation 2 gives equation 4:

$$a(x+\frac{1}{2}y) : \frac{1}{2}ay + \frac{1000}{798}a = 37.8 : 100 \qquad (4)$$

$$\therefore x+\frac{1}{2}y : \frac{1}{2}y + \frac{1000}{798} = 37.8 : 100$$

$$\therefore 37.8(\frac{1}{2}y + \frac{1000}{798}) = 100x + 50y$$

$$\therefore 100x + 31.1y = \frac{37800}{798} = 47.4 \qquad (5)$$

Since ***y*** is defined in terms of 1–***x***, the equation 5 can be re-written as:

$$100x + 31.1(1-x) = 47.4$$

$$\therefore 68.9x = 16.3$$

$$\therefore x = 0.24 \qquad (6)$$

$$\therefore y = 1 - x = 0.76 \qquad (7)$$

3.2.3.2. The influence of electronic properties of the indole backbone (Figure 5)

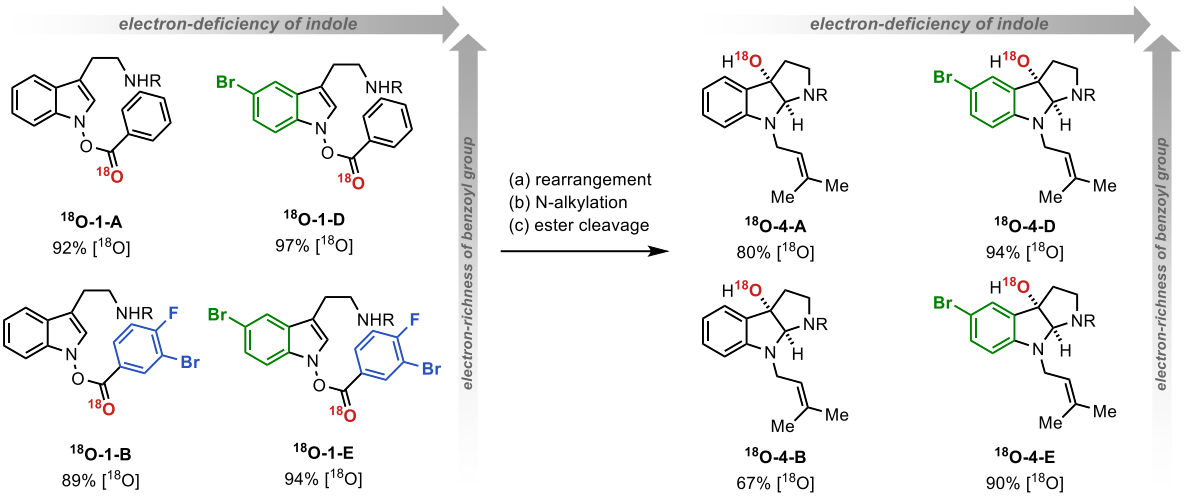
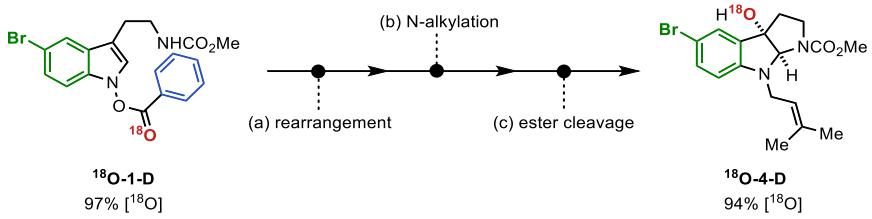


Figure S4. The influence of electronic properties of the indole backbone.

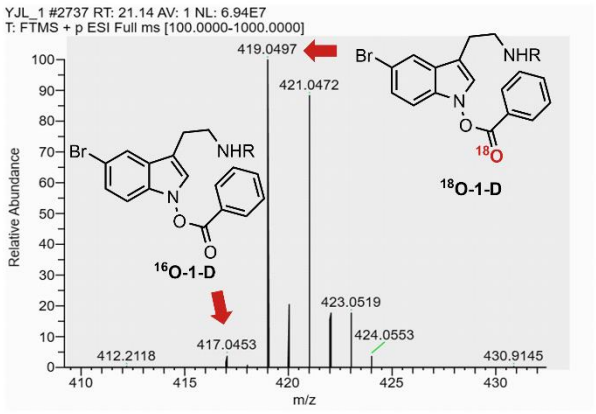
The determination of the relative contribution of **path b** and **path c** in each case was carried out via analogous calculations used for section **5.1.3.2.**

(1) **IHT** reaction with benzoyl substituent

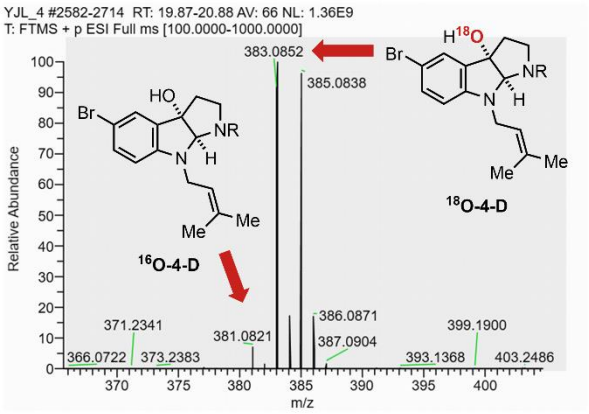


^{18}O-1-D
97% [^{18}O]

^{18}O-4-D
94% [^{18}O]



^{18}**O-1-D**:^{16}**O-1-D** = $a : b = 100 : 3.1$



^{18}**O-4-D**:^{16}**O-4-D** = $a(x+\frac{1}{2}y) : \frac{1}{2}ay+b = 100 : 7.0$

The system of equations is established by the two proportional expressions:

$$\begin{cases} a:b = 100:3.1 & (1) \\ a(x+\frac{1}{2}y):\frac{1}{2}ay+b = 100:7.0 & (2) \end{cases}$$

From equation 1, ***b*** can be expressed as:

$$b = \frac{31}{1000}a \qquad (3)$$

Insertion of the equation 3 into equation 2 gives equation 4:

$$\mathrm{a}(x+\frac{1}{2}y):\frac{1}{2}ay+\frac{31}{1000}a = 100:7.0 \qquad (4)$$

$$\therefore x+\frac{1}{2}y:\frac{1}{2}y+\frac{31}{1000} = 100:7.0$$

$$\therefore 50y+3.1 = 7x+3.5y$$

$$\therefore 7x-46.5y = 3.1 \qquad (5)$$

Since ***y*** is defined in terms of 1–***x***, the equation 5 can be re-written as:

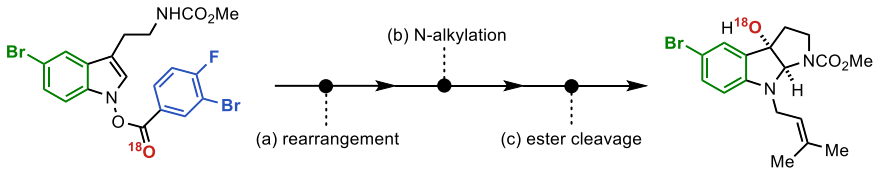
$$7x-46.5(1-x) = 3.1$$

$$\therefore 53.5x = 49.6$$

$$\therefore x = 0.93 \qquad (6)$$

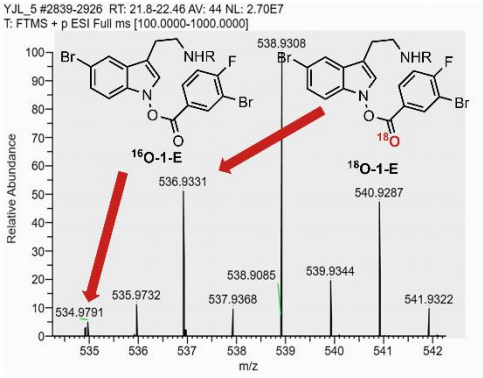
$$\therefore y = 1-x = 0.7 \qquad (7)$$

(2) **IHT** reaction with 3-bromo-4-fluorobenzoyl substituent

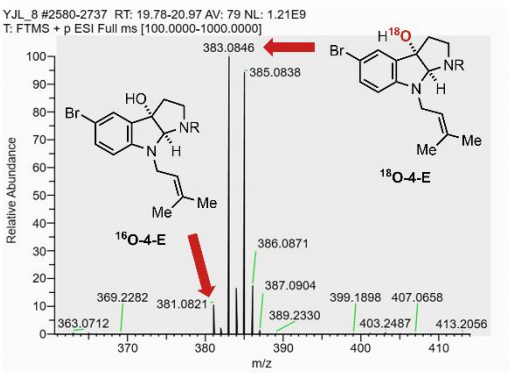


^{18}O-1-E
89% [^{18}O]

^{18}O-4-E
67% [^{18}O]



^{18}O-1-E:^{16}O-1-E = *a : b = 50.9 : 3.1*



^{18}O-4-E:^{16}O-4-E = $a(x+\frac{1}{2}y) : \frac{1}{2}ay+b = 100 : 10.6$

The system of equations is established by the two proportional expressions:

$$\begin{cases} a:b = 50.9:3.1 & (1) \\ a(x+\frac{1}{2}y):\frac{1}{2}ay+b = 100:10.6 & (2) \end{cases}$$

From equation 1, ***b*** can be expressed as:

$$b = \frac{31}{509}a \qquad (3)$$

Insertion of the equation 3 into equation 2 gives equation 4:

$$\mathrm{a}(x+\frac{1}{2}y):\frac{1}{2}ay+\frac{31}{509}a = 100:10.6 \qquad (4)$$

$$\therefore x+\frac{1}{2}y:\frac{1}{2}y+\frac{31}{509} = 100:10.6$$

$$\therefore 50\mathrm{y}+\frac{3100}{509} = 10.6x+5.3y$$

$$\therefore 10.6x-44.7y = \frac{3100}{509} \qquad (5)$$

Since ***y*** is defined in terms of 1–***x***, the equation 5 can be re-written as:

$$10.6x-44.7(1-\mathrm{x}) = \frac{3100}{509}$$

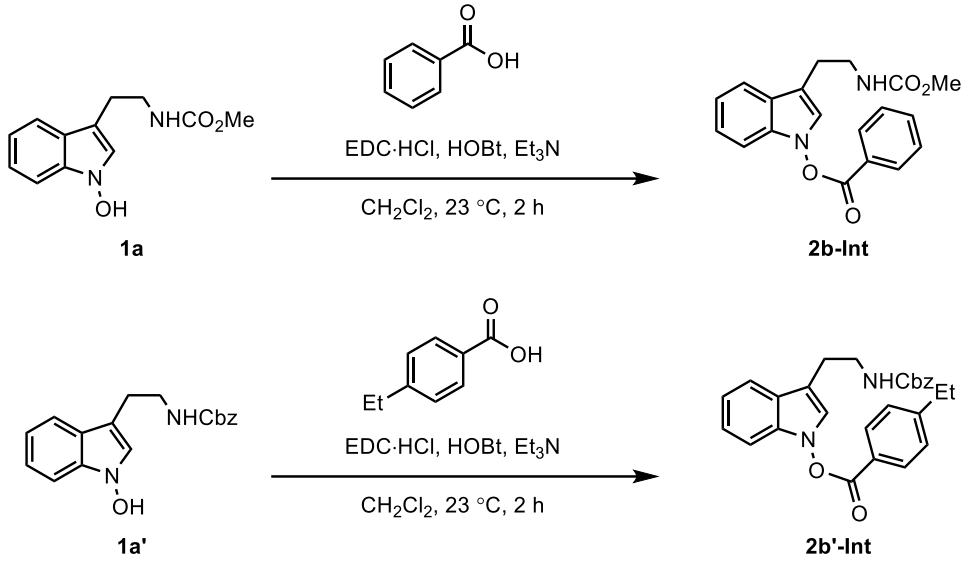
$$\therefore 55.3x = 50.8$$

$$\therefore x = 0.92 \qquad (6)$$

$$\therefore y = 1-x = 0.08 \qquad (7)$$

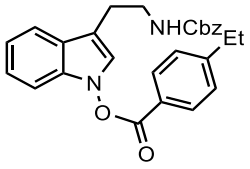
3.3. Crossover Experiment (Figure 6A)

3.3.1. Preparation of Compound 2b-Int and 2b'-Int



To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1** (1.0 equiv) and CH_2Cl_2 (0.05 M in **1**) at 23 °C, followed by benzoic acid (1.1 equiv), EDC·HCl (1.1 equiv), HOBt (1.1 equiv), and Et_3N (2.2 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H_2O. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1) to afford indolyl *N*-carboxylate **2-Int**.

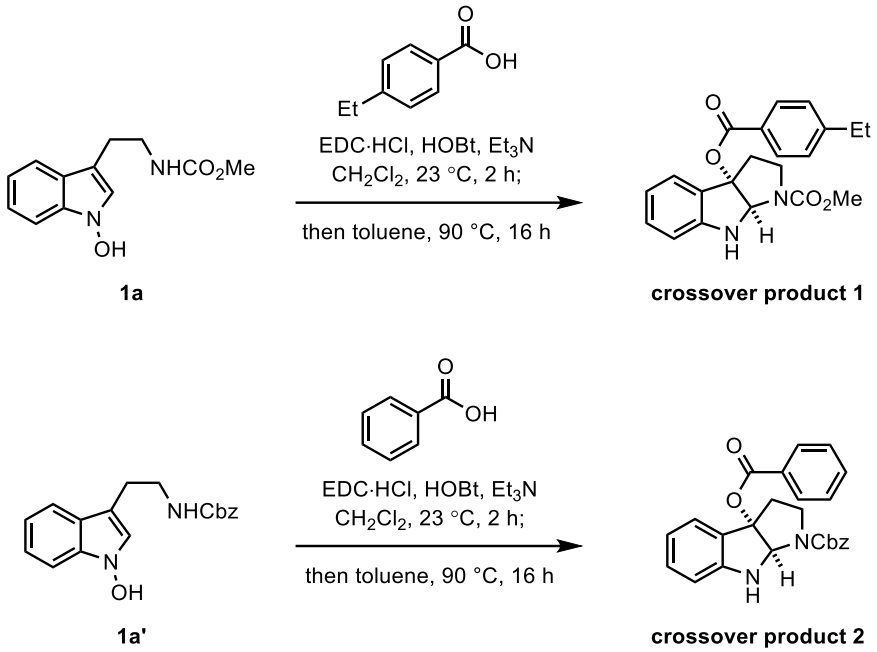
3-(2-(((Benzyloxy)carbonyl)amino)ethyl)-1H-indol-1-yl 4-ethylbenzoate (2b'-Int)



***R**f*=0.60 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.27 (m, 5H), 7.24 (d, *J* = 3.2 Hz, 2H), 7.16 (dt, *J* = 8.1, 3.8 Hz, 1H), 7.07 (s, 1H), 5.12 (s, 2H), 4.92 (s, 1H), 3.56 (q, *J* = 6.6 Hz, 2H), 2.99 (t, *J* = 6.8 Hz, 2H), 2.78 (q, *J* = 7.6 Hz, 2H), 1.31 (td, *J* = 7.6, 1.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 164.9, 156.5, 152.0, 136.8, 135.8, 130.6, 128.6,

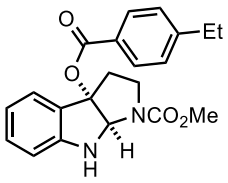
128.2, 128.2, 124.9, 124.2, 123.9, 123.6, 121.0, 119.4, 111.7, 109.2, 66.8, 41.2, 29.8, 29.3, 25.8, 15.3; **HRMS** calcd. for $C_{27}H_{27}N_2O_4^+$ $[M + H]^+$ 443.1965, found 443.1961.

3.3.2. Preparation of Crossover Products



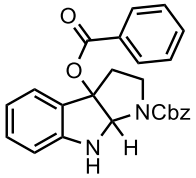
To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1** (1.0 equiv) and CH_2Cl_2 (0.05 M in **1**) at 23 °C, followed by benzoic acid (1.1 equiv), EDC·HCl (1.1 equiv), HOBt (1.1 equiv), and Et_3N (2.2 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H_2O. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude was filtered through a short pad of silica gel using CH_2Cl_2 as eluent, concentrated under reduced pressure and re-dissolved in toluene (0.05 M in **1**). The resulting solution was then heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to provide the crude product. The crude product was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product.

Methyl 3a-((4-ethylbenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (crossover product 1)



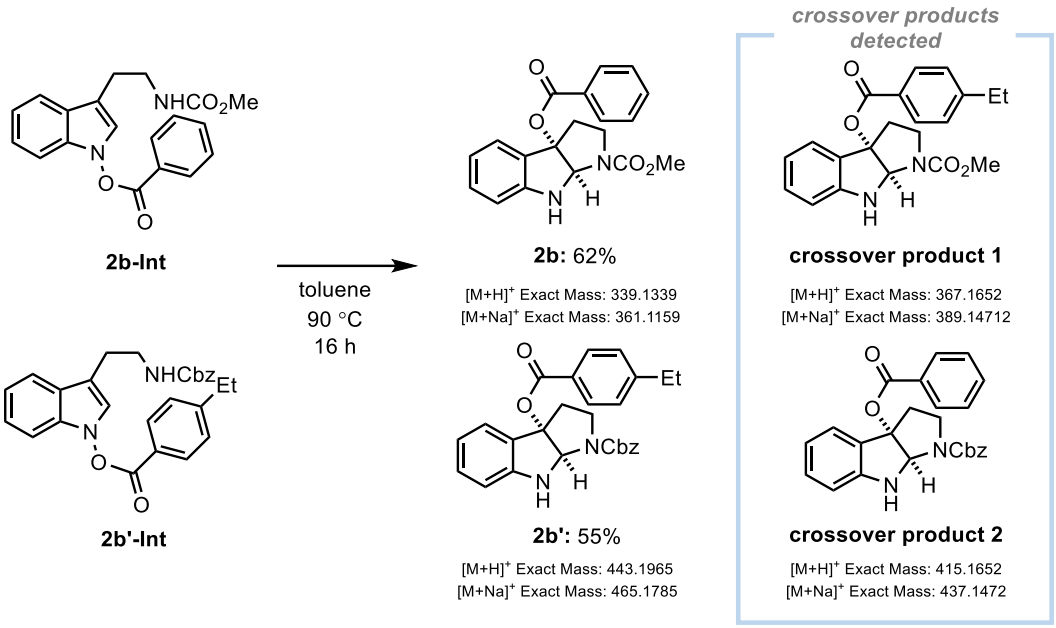
***R**f*=0.43 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.90 (d, *J* = 7.8 Hz, 2H), 7.62 and 7.54 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.79 (q, *J* = 6.8 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 5.77 (s, 1H), 3.92 and 3.81 (t, *J* = 9.7 Hz, 1H), 3.79 and 3.73 (s, 3H), 3.22 (td, *J* = 10.9, 6.3 Hz, 1H), 3.06 (dd, *J* = 12.9, 6.3 Hz, 1H), 2.94 (dd, *J* = 12.8, 6.1 Hz, 0H), 2.75 – 2.65 (m, 3H), 1.23 (t, *J* = 7.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.5, 155.7, 154.9, 151.0, 150.8, 150.3, 131.1, 130.0, 128.0, 127.7, 126.7, 126.3, 126.1, 126.1, 119.7, 119.5, 110.4, 110.3, 94.3, 93.1, 80.5, 79.7, 52.9, 52.7, 45.6, 45.5, 36.0, 35.8, 29.1, 15.4; **HRMS** calcd. for $C_{21}H_{23}N_2O_4^+$ $[M + H]^+$ 367.1652, found 367.1647.

Benzyl 3a-(benzoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (crossover product 2)



***R**f*=0.56 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$, 55:45 mixture of rotamers): δ 7.99 and 7.98 (d, *J* = 7.6 Hz, 2H), 7.63 and 7.55 (d, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 8.3 Hz, 1H), 7.44 – 7.28 (m, 7H), 7.19 (q, *J* = 6.7 Hz, 1H), 6.80 (t, *J* = 7.5 Hz, 2H), 6.69 and 6.63 (d, *J* = 7.9 Hz, 1H), 5.81 and 5.79 (s, 1H), 5.25 and 5.20 (d, *J* = 12.3 Hz, 1H), 5.21 and 5.12 (d, *J* = 12.3 Hz, 1H), 3.94 and 3.87 (t, *J* = 9.1 Hz, 1H), 3.32 – 3.20 (m, 1H), 3.07 and 2.98 (dd, *J* = 12.8, 5.3 Hz, 1H), 2.77 – 2.67 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.5, 165.4, 155.1, 154.3, 151.0, 150.7, 136.4, 134.4, 133.3, 133.3, 131.2, 131.1, 130.3, 130.2, 129.9, 129.9, 128.9, 128.7, 128.7, 128.5, 128.4, 128.3, 128.1, 126.7, 126.6, 126.2, 126.0, 126.0, 119.7, 119.5, 110.5, 110.3, 94.4, 93.3, 80.5, 79.7, 67.6, 67.2, 45.7, 45.6, 35.9, 35.8; **HRMS** calcd. for $C_{25}H_{23}N_2O_4^+$ $[M + H]^+$ 415.1652, found 415.1648.

3.3.3. Crossover Experiment

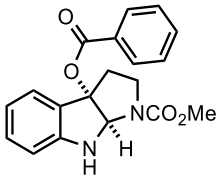


To a 10 mL oven-dried reaction tube equipped with a stir bar were added **2b-Int** (67.6 mg, 0.200 mmol, 1.0 equiv), **2b'-Int** (88.5 mg, 0.200 mmol, 1.0 equiv) and toluene (2 mL). The reaction tube was sealed under N_2 and the resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to provide the crude product. A small portion of the crude mixture was then analyzed by TLC and HRMS. The crude mixture of crossover experiment was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product **2b** (41.7 mg, 62%) and **2b'** (48.9 mg, 55%).

From the TLC analysis, no appreciable amount of crossover products was detected.

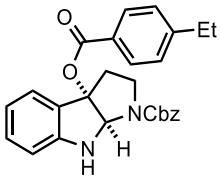
As a result of comparing the retention times of individually synthesized compounds by HPLC analysis performed simultaneously with HRMS analysis, it was concluded that **crossover product 1** and **crossover product 2** were not detected.

Methyl 3a-(benzoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2b)



The spectral data matched to those of compound **^{18}O-2-A** (See section 3.2.1.1.). R_f =0.38 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$s): δ 7.99 (d, *J* = 7.7 Hz, 2H), 7.63 and 7.58 (d, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 8.4 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.7 Hz, 1H), 6.80 (q, *J* = 7.0 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 5.78 (s, 1H), 3.93 and 3.81 (t, *J* = 9.7 Hz, 1H), 3.80 and 3.73 (s, 3H), 3.26 – 3.20 (m, 1H), 3.07 and 2.96 (dd, *J* = 12.9, 6.1 Hz, 1H), 2.75 – 2.69 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.3, 155.6, 154.8, 151.0, 150.7, 133.2, 131.0, 130.2, 129.8, 129.1, 128.4, 126.5, 126.3, 126.1, 126.0, 119.6, 119.3, 110.3, 110.2, 94.5, 93.3, 80.4, 79.6, 52.8, 52.5, 45.5, 35.9, 35.8 ; **HRMS** calcd. for $C_{19}H_{18}N_2O_4Na^+$ $[M + Na]^+$ 361.1159, found 361.1160.

3-(2-(((Benzyloxy)carbonyl)amino)ethyl)-1H-indol-1-yl 4-ethylbenzoate (2b')



R_f=0.76 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.89 (dd, *J* = 8.2, 3.8 Hz, 2H), 7.62 and 7.54 (d, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 6.8 Hz, 1H), 7.36 (d, *J* = 4.4 Hz, 2H), 7.40 – 7.30 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.18 (tdd, *J* = 7.2, 5.6, 1.3 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.68 and 6.63 (d, *J* = 7.9 Hz, 1H), 5.80 and 5.78 (s, 1H), 5.24 and 5.20 (d, *J* = 12.2 Hz, 1H), 5.20 and 5.12 (d, *J* = 12.3 Hz, 1H), 3.93 and 3.87 (ddd, *J* = 10.6, 8.5, 1.8 Hz, 1H), 3.30 – 3.20 (m, 1H), 3.06 and 2.96 (ddd, *J* = 12.8, 6.4, 1.8 Hz, 1H), 2.76 – 2.68 (m, 1H), 2.68 (q, *J* = 7.5 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.5, 155.1, 154.3, 151.0, 150.7, 150.3, 150.3, 136.5, 131.1, 130.0, 128.9, 128.8, 128.5, 128.4, 128.3, 128.1, 128.0, 127.7, 127.7, 126.7, 126.2, 126.1, 119.7, 119.5, 110.4, 110.3, 94.2, 93.1, 80.5, 79.7, 67.5, 67.2, 45.7, 45.6, 35.9, 35.8, 29.1, 15.4; **HRMS** calcd. for $C_{27}H_{27}N_2O_4^+$ $[M + H]^+$ 443.1965, found 443.1964.

3.3.4. Analysis of Crossover Experiment Results

3.3.4.1. TLC analysis of the crossover experiment

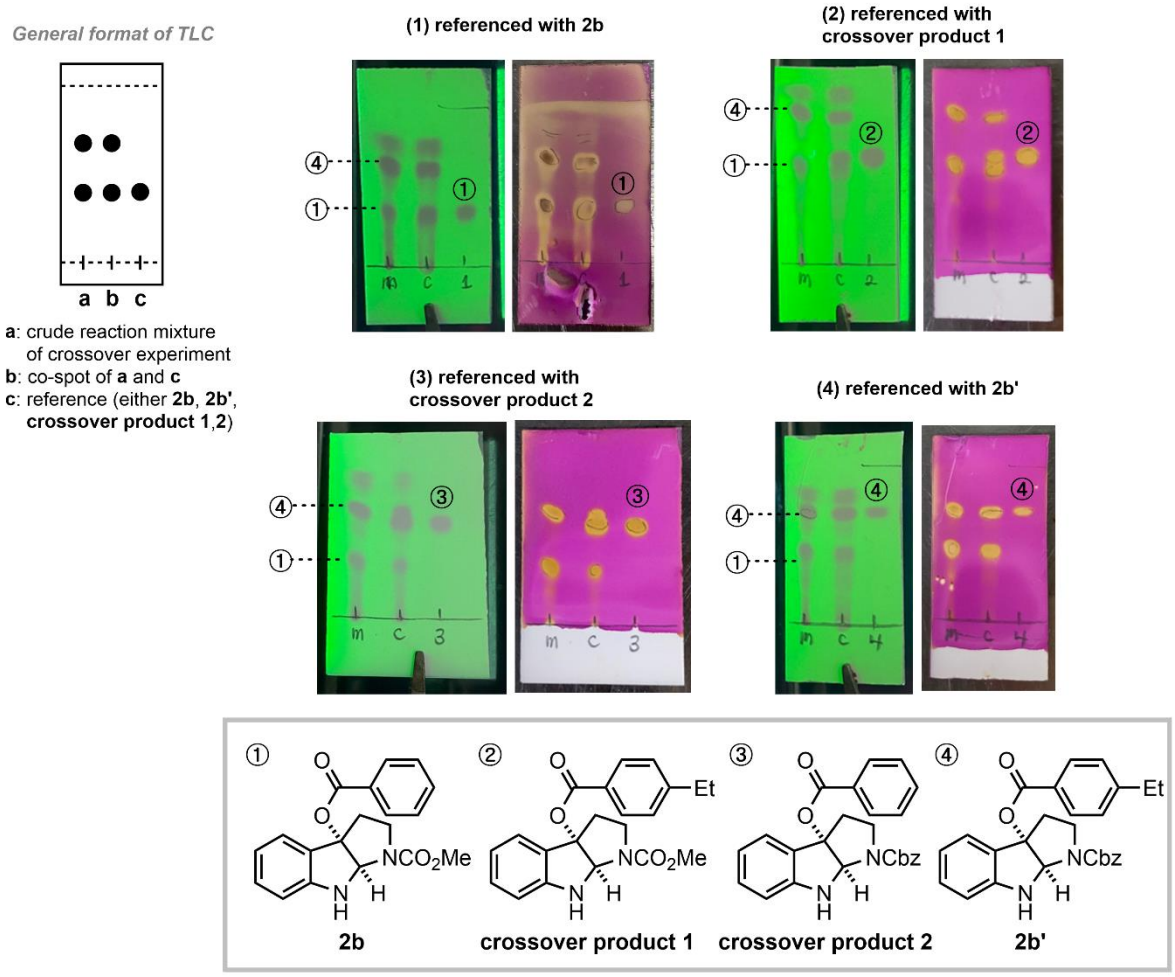
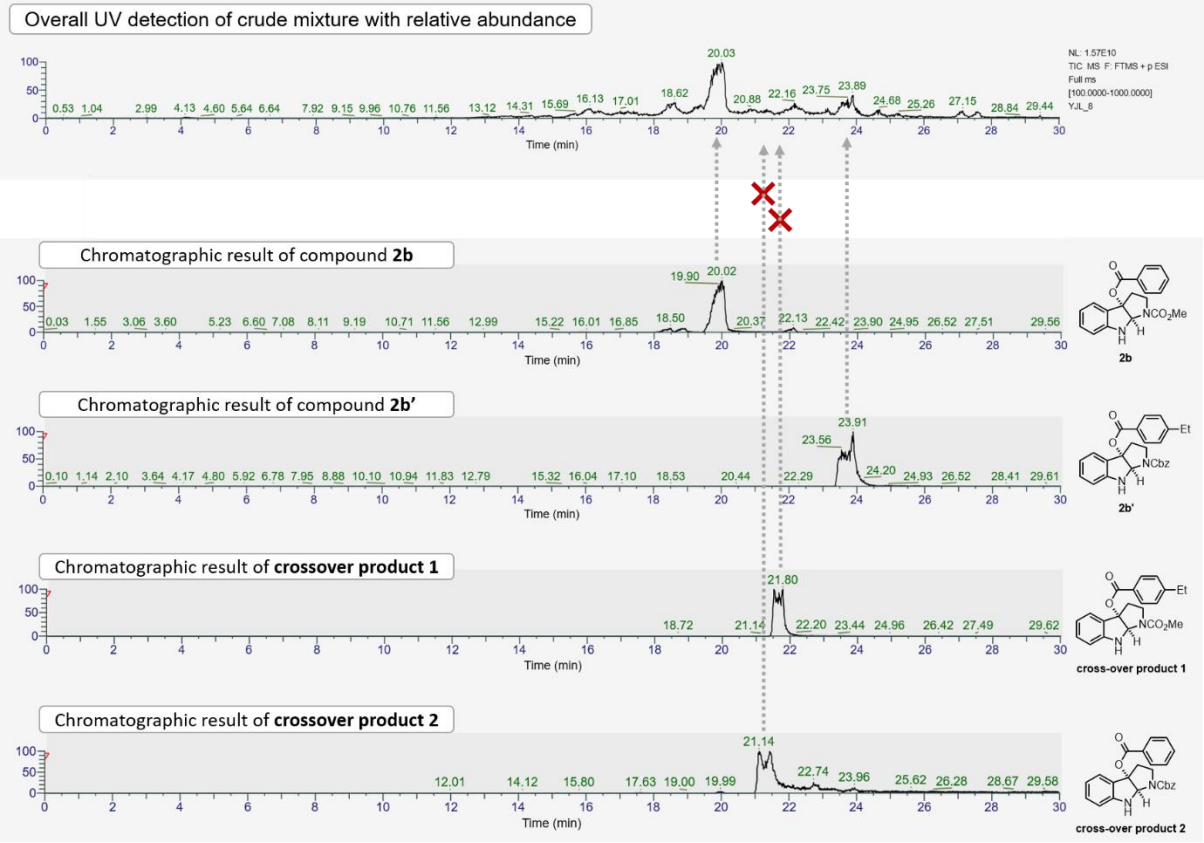


Figure S5. TLC analysis of crossover experiment.

TLC was checked with the reference compounds, which are the pyrroloindoline **2b**, **2b', crossover product 1,** and **crossover product 2.** Each TLC sample was visualized by 254 nm UV lamp and stained with $KMnO_4$ stain with heating. Among the photos of the TLC plates with two differently visualized forms, the one visualized by 254 nm UV lamp is on the left and the one stained with $KMnO_4$ is on the right. TLC analysis indicates that no detectable spots corresponding to the **crossover product 1**, **2** were observed in each TLC while formation of **2b** and **2b'** was clearly detected.

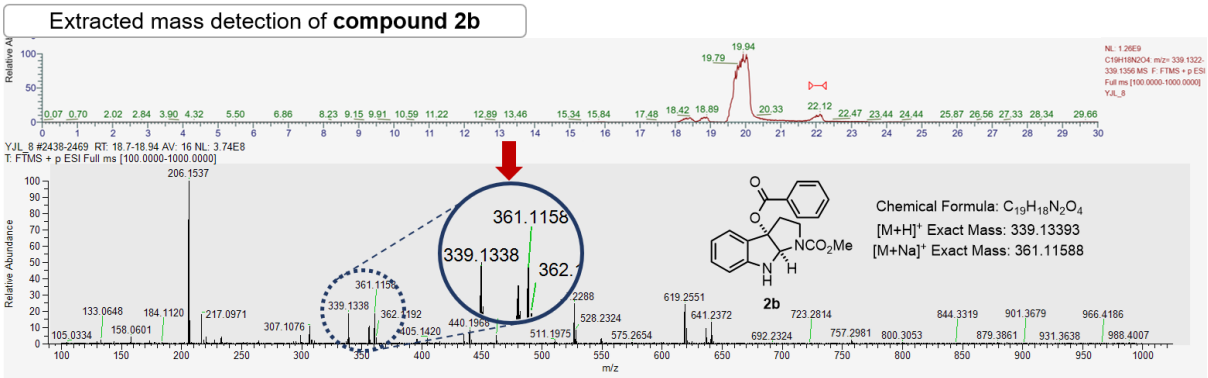
3.3.4.2. HRMS/HPLC analysis of the crossover experiment

(1) Result of UV detection for the crude mixture of the crossover experiment and the relative location of each product

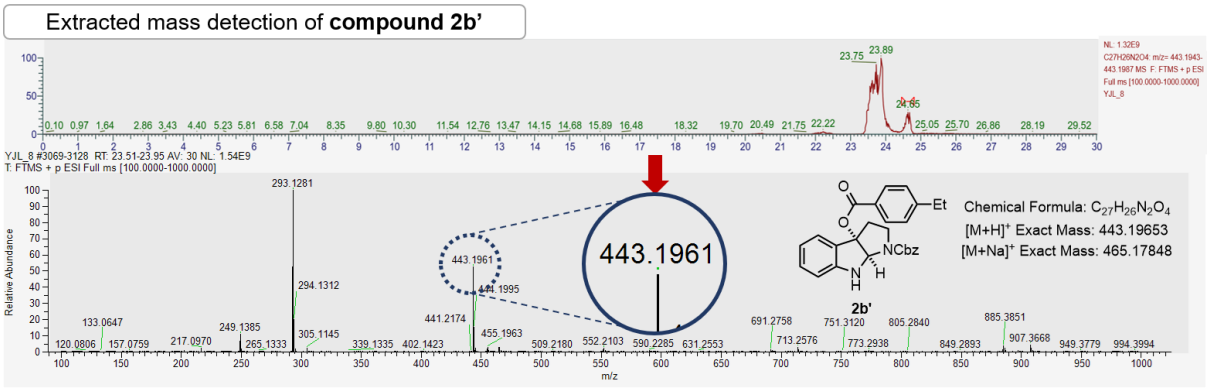


For all HRMS peaks shown below, the red arrow was used to indicate the detected mass of the desired products.

(2) Result of mass detection at peak corresponding to compound **2b**

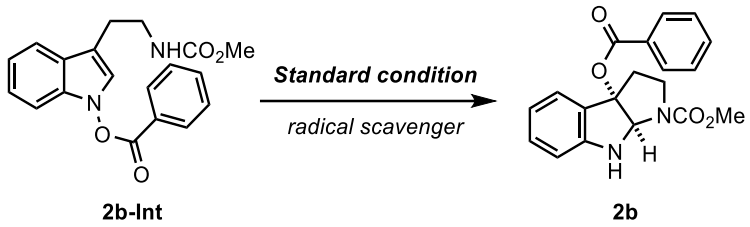


(3) Result of mass detection at peak corresponding to compound **2b'**



3.4. Radical-trapping Experiment (Figure 6B)

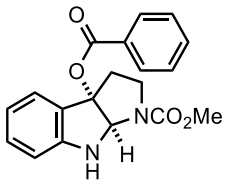
3.4.1. Radical-trapping Experiment with Indolyl *N*-Carboxylate 2b-Int



2b-Int

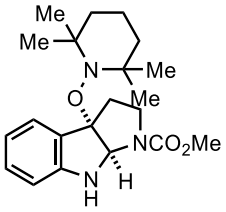
2b

scavengers	2b
TEMPO	54%
BHT	65%
1,1-diphenylethylene	57%
none	68%



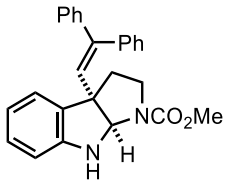
2b

[M+H]$^+$ Exact Mass: 339.1339
[M+Na]$^+$ Exact Mass: 361.1159



TEMPO-adduct

[M+H]$^+$ Exact Mass: 374.2438
[M+Na]$^+$ Exact Mass: 396.2258

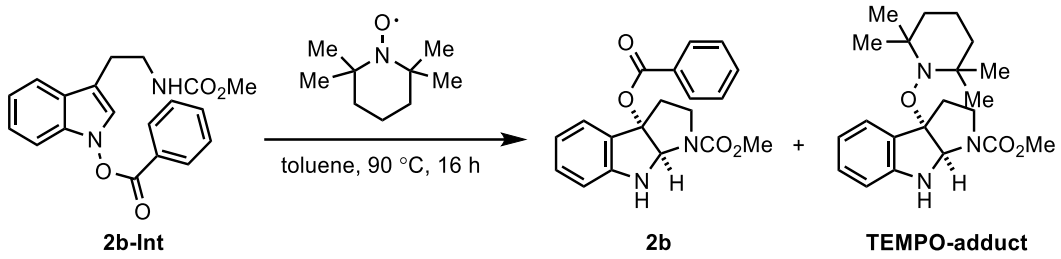


1,1-diphenylethylene-adduct

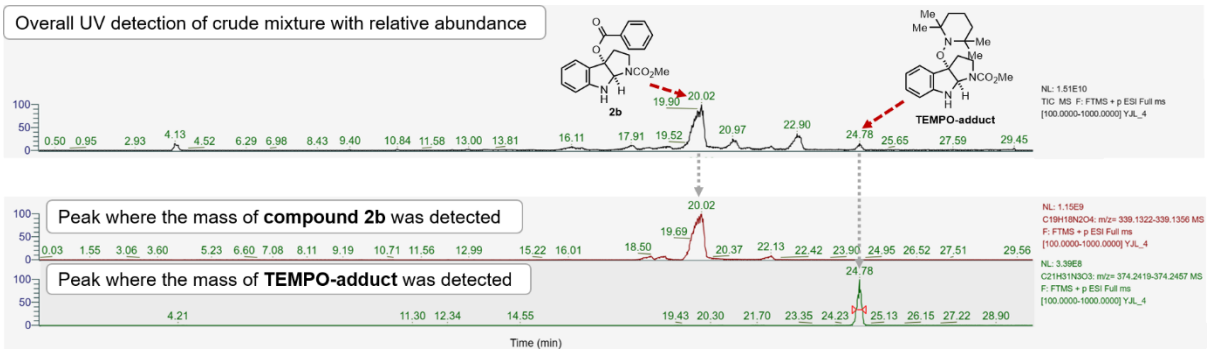
[M+H]$^+$ Exact Mass: 397.1911
[M+Na]$^+$ Exact Mass: 419.1730

To a 10 mL oven-dried reaction tube equipped with a stir bar were added indolyl *N*-carboxylate **2b-Int** (67.6 mg, 0.200 mmol, 1.0 equiv) and toluene (4 mL, 0.05 M in **2b-Int**) at 23 °C, followed by radical-trapping reagent (2.0 equiv). The reaction tube was sealed under N_2 and the resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to provide the crude product. The crude mixture was then analyzed by HRMS. HRMS result of the resulting crude mixture indicated the formation of **TEMPO-adduct** or **1,1-diphenylethylene-adduct** when TEMPO or 1,1-diphenylethylene were used as a radical scavenger, even though no significant yield loss was observed for **2b.** Each crude mixture of radical-trapping experiment was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1) to afford the product **2b** (when using TEMPO: 40.3 mg, 54%, when using BHT: 44.1 mg, 65%, when using 1,1-diphenylethylene: 38.6 mg, 57%)

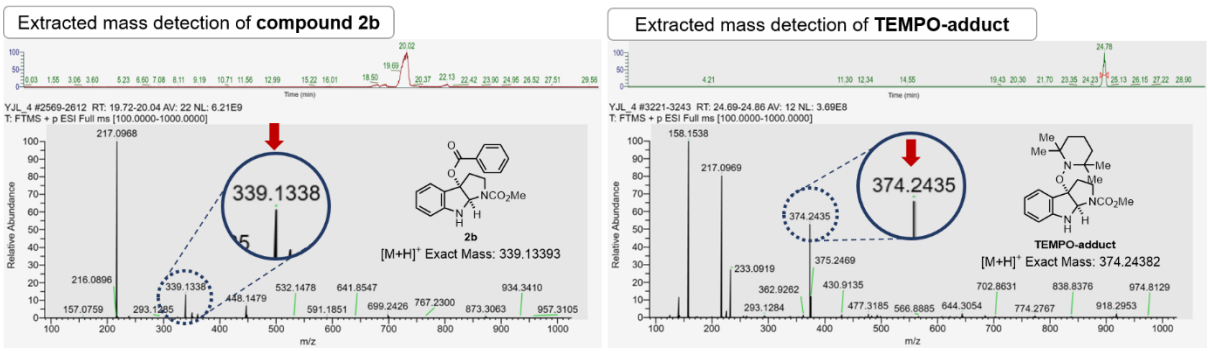
3.4.1.1. HRMS results using TEMPO as a radical scavenger



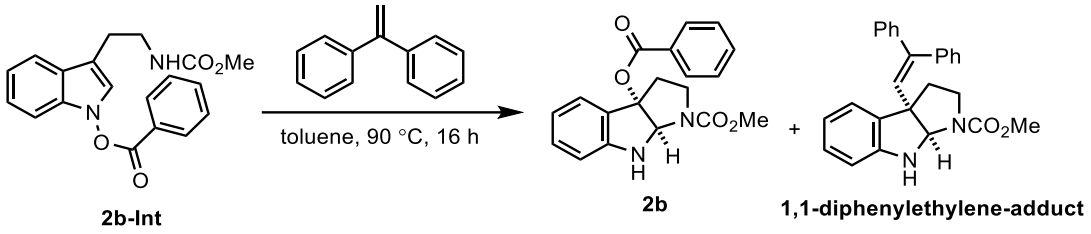
(1) Result of UV detection for the radical-trapping experiment and the relative location of each product detected



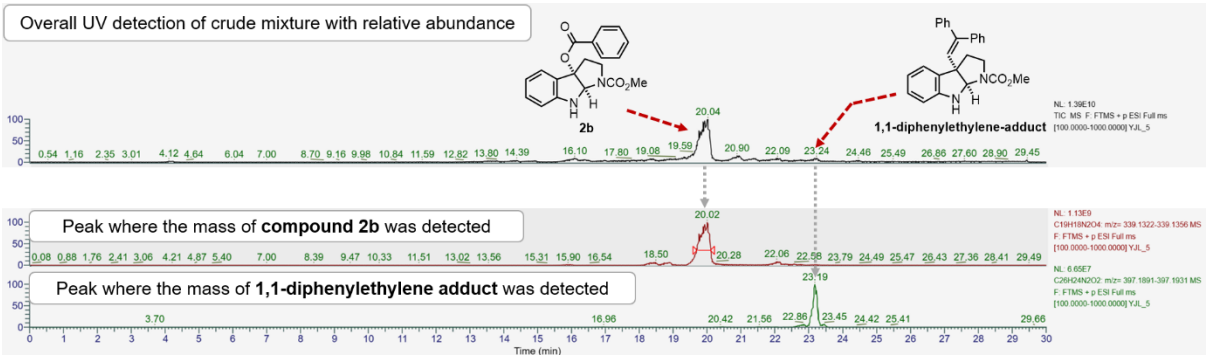
(2) Result of mass detection at peaks corresponding to compound **2b** and **TEMPO-adduct**



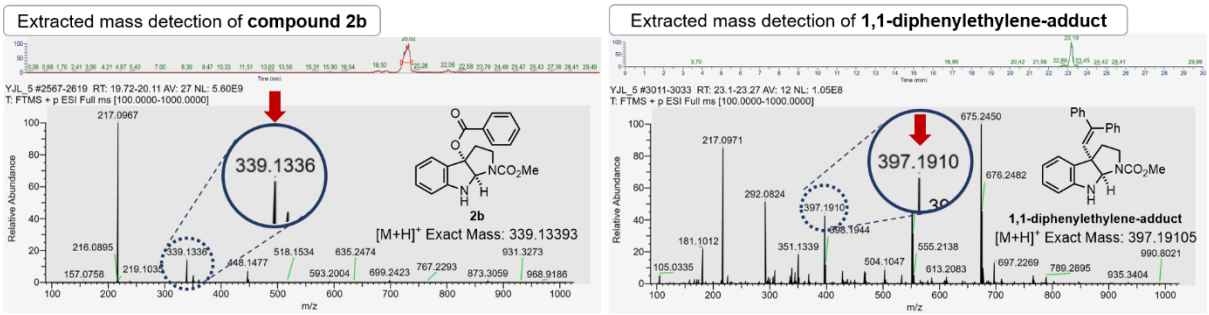
3.4.1.2. HRMS results using 1,1-diphenylethylene as a radical scavenger



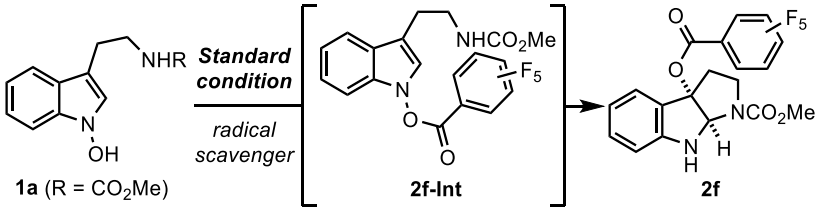
(1) Result of UV detection for the radical-trapping experiment and the relative location of each product detected



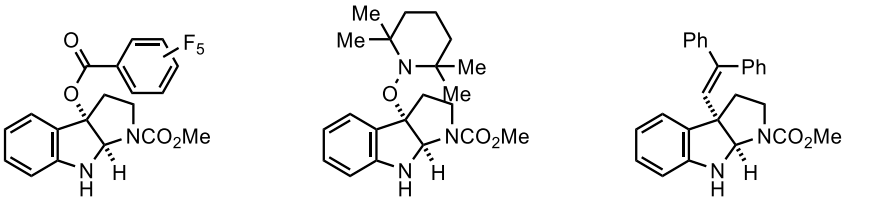
(2) Result of mass detection at peaks corresponding to compound **2b** and **1,1-diphenylethylene-adduct**



3.4.2. Radical-trapping Experiment with Electron-deficient Indolyl *N*-Carboxylate



scavengers	2f
TEMPO	0%
BHT	49%
1,1-diphenylethylene	45%
none	53%



2f

$[M+H]^+$ Exact Mass: 429.0868
$[M+Na]^+$ Exact Mass: 451.0688

TEMPO-adduct

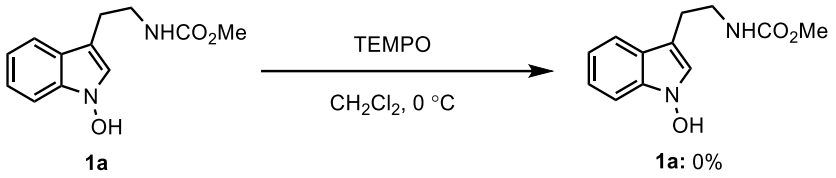
$[M+H]^+$ Exact Mass: 374.2438
$[M+Na]^+$ Exact Mass: 396.2258

1,1-diphenylethylene-adduct

$[M+H]^+$ Exact Mass: 397.1911
$[M+Na]^+$ Exact Mass: 419.1730

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1a** (50.0 mg, 0.213 mmol, 1.0 equiv) and CH_2Cl_2 (4.2 mL, 0.05 M in **1a**) at 23 °C. The resulting solution was cooled to 0 °C and 2,3,4,5,6-pentafluorobenzoyl chloride (1.1 equiv), Et_3N (1.1 equiv) and radical-trapping reagent (2.0 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was quenched with H_2O (2 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to provide the crude product. The crude mixture was then analyzed by HRMS. When 1,1-diphenylethylene was used as the radical scavenger, **1,1-diphenylethylene-adduct** was detected by HRMS analysis, while no significant decrease in the reaction yield was observed. On the other hand, the formation of **2f** was noticeably suppressed when TEMPO was used as the radical scavenger due to the rapid decomposition of **1a** induced by TEMPO. Each crude mixture of radical-trapping experiment was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1) to afford the product **2f** (when using TEMPO: 0 mg, 0%, when using BHT: 44.7 mg, 49%, when using 1,1-diphenylethylene: 41.1 mg, 45%)

3.4.2.1. Instability of 1a in the presence of TEMPO

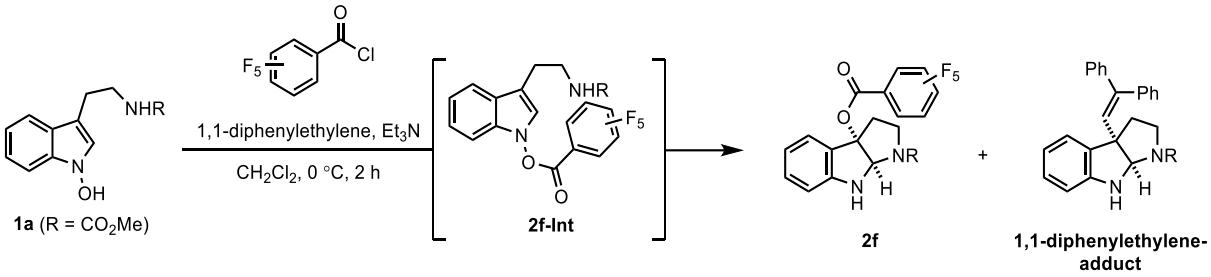


1a **1a:** 0%

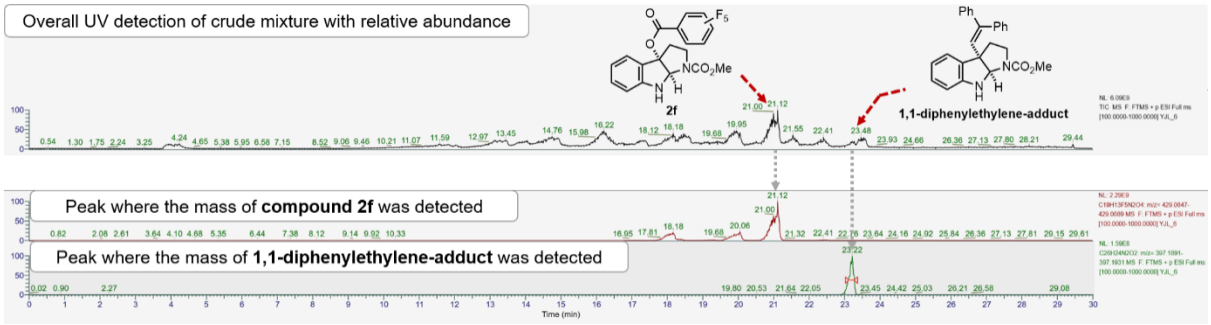
*Fast decomposition of **1a** was observed*

To confirm that the TEMPO is interacting with the *N*-hydroxyindole, *N*-hydroxyindole **1a** (50.0 mg, 0.213 mmol, 1.0 equiv) and CH_2Cl_2 (4.2 mL, 0.05 M in **1a**) were added to an oven-dried round-bottom flask equipped with a stir bar and septum at 23 °C. The resulting solution was cooled to 0 °C, and TEMPO (2.0 equiv) was added to the solution. The reaction mixture was stirred while the reaction was monitored by TLC. TLC indicated that fast decomposition of **1a** occurred immediately after TEMPO was added. This clearly indicates that the result of radical-trapping experiment with TEMPO is derived from the decomposition of **1a**, not from the inhibition of the radical-involved reaction pathway.

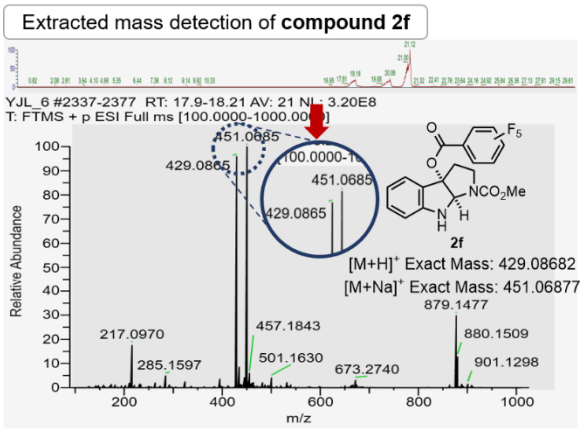
3.4.2.2. HRMS results using 1,1-diphenylethylene as a radical scavenger

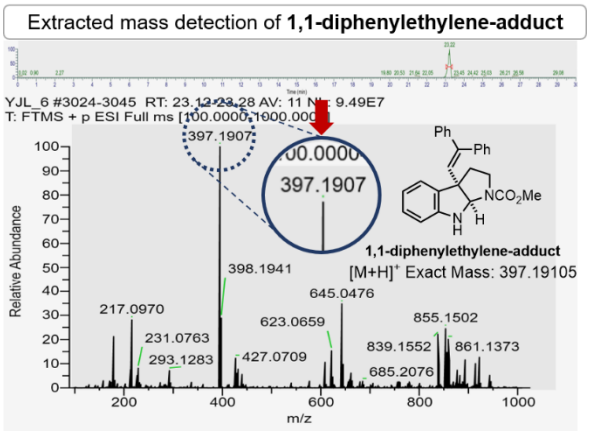


(1) Result of UV detection for the radical-trapping experiment and the relative location of each product detected



(2) Result of mass detection at peaks corresponding to compound **2f** and **1,1-diphenylethylene-adduct**

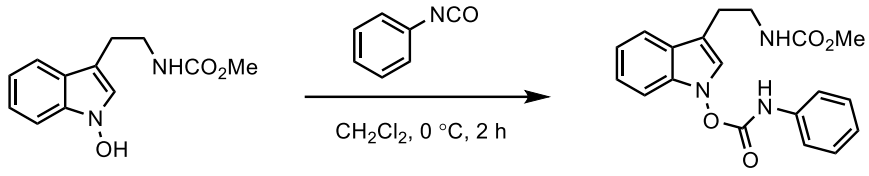




3.5. IHT Reaction of Indolyl *N*-Carbamates (Figure 7)

3.5.1. Preparation of Indolyl *N*-Carbamates

Methyl (2-(1-((phenylcarbamoyl)oxy)-1H-indol-3-yl)ethyl)carbamate (2g-Int)

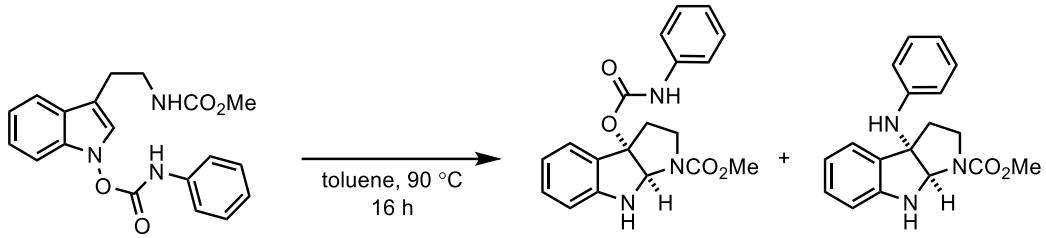


1a **2g-Int**

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1a** (318 mg, 1.36 mmol, 1.0 equiv) and CH_2Cl_2 (14 mL, 0.1 M in **1a**) at 23 °C. The resulting solution was cooled to 0 °C, and phenyl isocyanate (155 μL, 1.42 mmol, 1.04 equiv) was added to the solution. The reaction mixture was stirred for 2 h, before it was quenched with H_2O (10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was washed with brine (1 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford indolyl *N*-carboxylate **2g-Int** (336 mg, 70%) as a pale yellow oil.

***R*$_f$**=0.47 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.33 – 7.26 (m, 2H), 7.17 (q, *J* = 7.1 Hz, 2H), 7.06 (s, 1H), 4.84 (s, 1H), 3.66 (s, 3H), 3.52 (q, *J* = 6.7 Hz, 2H), 2.95 (t, *J* = 6.9 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.4, 151.8, 136.7, 135.7, 129.3, 124.7, 124.6, 124.0, 123.6, 122.2, 121.0, 119.3, 119.1, 111.5, 111.4, 109.0, 52.2, 41.1, 25.7; **HRMS** calcd. for $C_{19}H_{20}N_3O_4^+$ $[M + H]^+$ 354.1448, found 354.1445.

3.5.2. IHT Reaction of Indolyl *N*-Carbamate 2g-Int



2g-Int **2g:** 27% **2h:** 18%

To a 10 mL oven-dried reaction tube equipped with a stir bar were added indolyl *N*-carboxylate **2g-Int** (0.120 g, 0.340 mmol, 1.0 equiv) and toluene (7 mL, 0.05 M in **2g-Int**) at 23 °C. The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to provide the crude product. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product **2g** and **2h** (**2g**: 32.4 mg, 27%, **2h**: 18.9 mg, 18%) as a pale yellow oil.

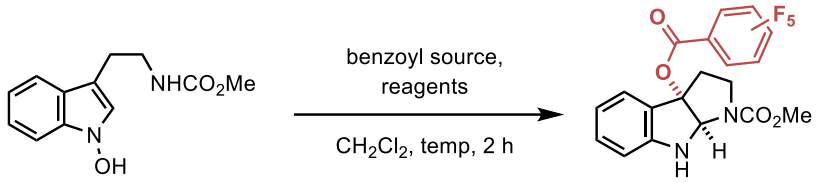
2g: R_f=0.47 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.61 and 7.53 (d, *J* = 7.6 Hz, 1H), 7.36 – 7.26 (m, 5H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.1 Hz, 1H), 6.81 (q, *J* = 7.4 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.65 – 6.61 (m, 1H), 5.68 and 5.63 (s, 1H), 5.21 and 4.85 (s, 1H), 3.89 and 3.79 (t, *J* = 9.8 Hz, 1H), 3.79 and 3.72 (s, 3H), 3.18 (td, *J* = 10.9, 6.3 Hz, 1H), 3.00 and 2.85 (dd, *J* = 12.9, 6.4 Hz, 1H), 2.70 (p, *J* = 11.6 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 155.7, 154.9, 152.0, 151.9, 150.9, 150.6, 137.7, 137.6, 131.2, 129.2, 126.6, 126.0, 125.9, 123.8, 119.8, 119.6, 119.0, 110.5, 110.4, 94.1, 92.8, 80.4, 79.6, 52.9, 52.7, 45.8, 45.6, 35.7, 35.5; **HRMS** calcd. for $C_{19}H_{20}N_3O_4^+$ $[M + H]^+$ 354.1448, found 354.1445.

2h: R_f=0.45 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.18 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.10 (t, *J* = 7.0 Hz, 2H), 6.77 (q, *J* = 7.1 Hz, 1H), 6.72 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 6.51 (dd, *J* = 11.4, 8.0 Hz, 2H), 5.73 and 5.69 (s, 1H), 5.14 and 4.80 (s, 1H), 4.05 and 4.00 (s, 1H), 3.85 and 3.74 (ddd, *J* = 11.5, 7.7, 3.7 Hz, 1H), 3.76 and 3.73 (s, 3H), 3.27 (ddd, *J* = 19.8, 16.6, 9.3 Hz, 1H), 2.63 (ddt, *J* = 30.8, 12.8, 8.5 Hz, 1H), 2.37 – 2.29 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 156.0, 155.3, 149.1, 148.9, 145.10, 145.09, 129.9, 129.4, 129.3, 123.6, 123.5, 119.6, 119.4, 118.7, 118.5, 115.5, 115.2, 109.9, 109.7, 73.6, 72.4, 52.9, 52.7, 44.8, 44.6, 37.8, 37.6; **HRMS** calcd. for $C_{18}H_{20}N_3O_2^+$ $[M + H]^+$ 310.1550, found 310.1546.

4. C–O Bond Formation via Indolyl 1,3-Heteroatom Transposition (IHT)

4.1. Optimization of the C3-Acyloxylation Conditions

Table S2. Evaluation of esterification conditions for pentafluorobenzoyl sources.[a]



1a **2f**

entry	benzoyl source	conditions	temperature	yield of 2f (%)[b]
1	C_6F_5COOH	EDC·HCl (1.1 equiv), HOBt (1.1 equiv), Et_3N (2.2 equiv)	23 °C	31%
2	C_6F_5COOH	DCC (1.1 equiv), DMAP (1.1 equiv)	23 °C	27%
3	C_6F_5COCl	Et_3N (1.2 equiv)	23 °C	38%
4	**C_6F_5COCl**	**Et_3N (1.2 equiv)**	**0 to 23 °C**	**55%**

[a]Reactions performed with *N*-hydroxyindole **1a** (1.0 equiv), benzoyl source (1.1 equiv) in CH_2Cl_2 (0.05 M) at indicated temperature on 0.5−1.0 mmol scale. [b]Yields were determined by ^1H NMR using TCE as an internal standard.

4.2. General Procedures for C3-Acyloxylation of Indole Derivatives (Scheme 2)

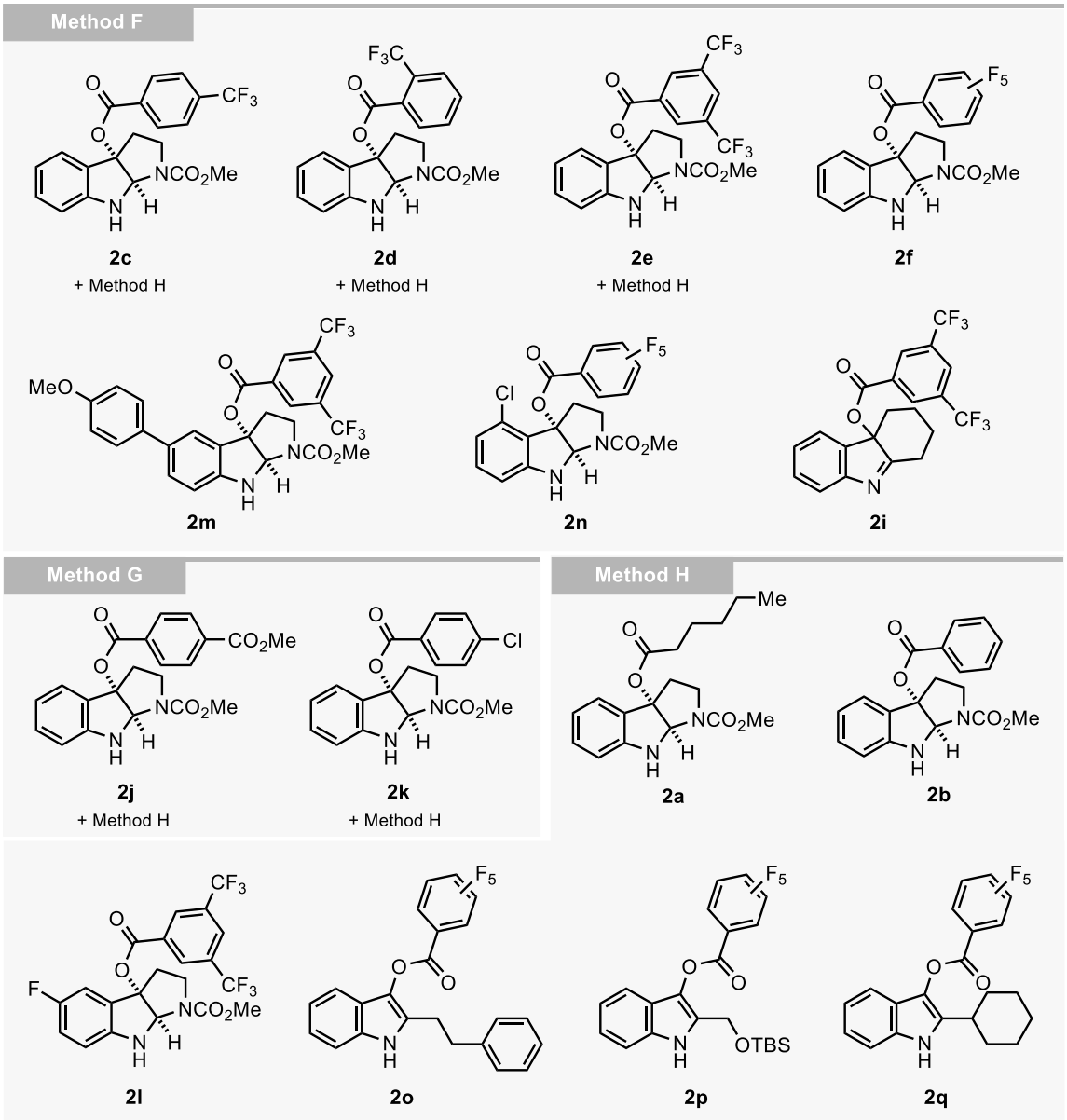
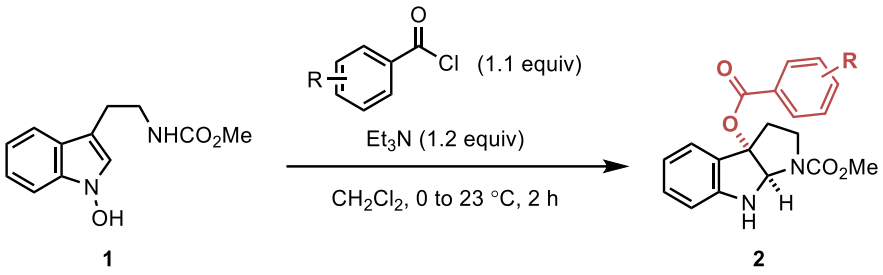


Figure S6. List of C3-acyloxylated products categorized by methods of C3-acyloxylation.

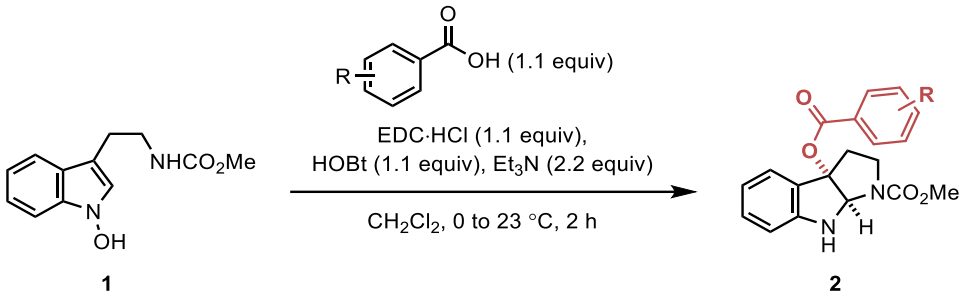
General procedure F



1 2

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1** (1.0 equiv) and CH_2Cl_2 (0.05 M in **1**) at 23 °C. The resulting solution was cooled to 0 °C, and benzoyl chloride (1.1 equiv) and Et_3N (1.2 equiv) were added to the solution at the same time. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was quenched with H_2O. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the product **2**.

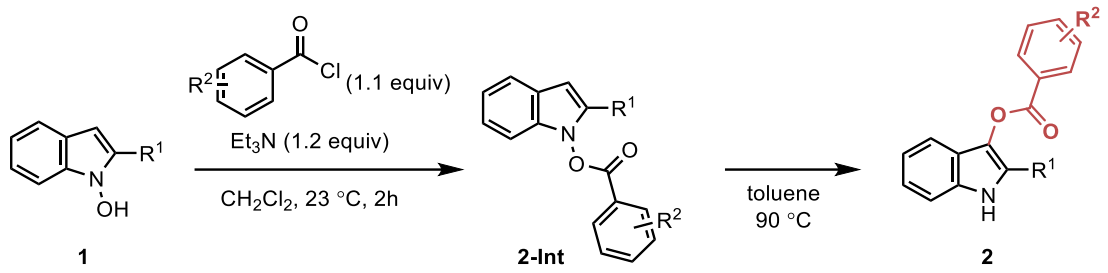
General procedure G



1 2

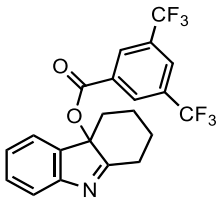
To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1** (1.0 equiv) and CH_2Cl_2 (0.05 M in **1**) at 23 °C. The resulting solution was cooled to 0 °C, and benzoic acid (1.1 equiv), EDC·HCl (1.1 equiv), HOBt (1.1 equiv) and Et_3N (2.2 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was quenched with H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the product **2**.

General procedure H



To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1** (1.0 equiv) and CH_2Cl_2 (0.05 M in **1**) at 23 °C, followed by benzoyl chloride (1.1 equiv) and Et_3N (1.2 equiv). The resulting mixture was stirred for 2 h, before it was quenched with $NaHCO_3$ (20 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with $NaHCO_3$ (sat. aq.), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude was filtered through a short pad of silica gel using CH_2Cl_2 as eluent, concentrated under reduced pressure and re-dissolved in toluene (0.05 M in **1**). The resulting solution was then heated to 90 °C in a pre-heated oil bath and stirred while the reaction was monitored by TLC. After completion of reaction (2−16 h), the reaction mixture was cooled to 23 °C, the crude mixture was concentrated under reduced pressure and directly purified by column chromatography to afford the product **2**.

1,2,3,4-Tetrahydro-4aH-carbazol-4a-yl 3,5-bis(trifluoromethyl)benzoate (2i)

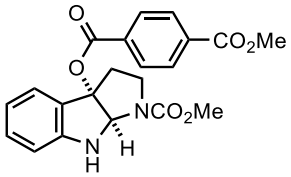


Following the **general procedure G**, *N*-hydroxyindole **1s** (86.6mg, 0.463 mmol) afforded indolenine **2i** (85.0 mg, 43%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1).

***R**f*=0.27 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.45 (s, 2H), 8.08 (s, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.43 – 7.40 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 3.00 (d, *J* = 15.0 Hz, 2H), 2.51 (td, *J* = 13.2, 5.9 Hz, 1H), 2.22 (br d, *J* = 10.9 Hz, 1H), 1.90 (tt, *J* = 13.3, 3.5 Hz, 1H), 1.85 – 1.81 (m, 1H), 1.62 – 1.49 (m, 1H), 1.36

(td, J = 14.1, 4.1 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 182.3, 161.7, 154.3, 137.2, 132.6 (q, J = 34.2 Hz), 131.7, 130.3, 130.0, 129.9, 126.9 (p, J = 3.8 Hz), 126.0, 122.9 (d, J = 273.0 Hz), 122.0, 121.2, 87.7, 38.4, 30.0, 28.6, 21.0; **^{19}F NMR** (471 MHz, $CDCl_3$): δ −63.0; **HRMS** calcd. for $C_{12}H_{16}N^+$ $[M + H]^+$ 174.1279, found 174.1277.

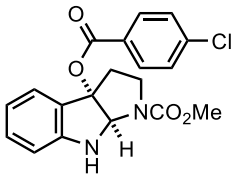
1-(Methoxycarbonyl)-2,3,8,8a-tetrahydropyrrolo[2,3-b]indol-3a(1H)-yl methyl terephthalate (2j)



Following the **general procedure G**, *N*-hydroxyindole **1a** (91.2 mg, 0.389 mmol) afforded an inseparable mixture of pyrroloindoline **2j-Int** and indolyl *N*-carboxylate **2j** (122 mg, 2.7:1, overall 79%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3). When following the **general procedure H** for 4 h, *N*-hydroxyindole **1a** (71.0 mg, 0.303 mmol) afforded pyrroloindoline **2j** (81.7 mg, 68%) as a sole product.

***R**$_f$*=0.27 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.06 (m, 1H), 7.62 and 7.56 (d, J = 7.5 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 6.84 – 6.76 (m, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.78 (s, 1H), 3.96 – 3.91 and 3.85 – 3.80 (m, 1H), 3.94 (s, 3H), 3.80 and 3.73 (s, 3H), 3.27 – 3.20 (m, 1H), 3.08 and 2.99 (dd, J = 12.8, 6.2 Hz, 1H), 2.72 (q, J = 10.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.3, 164.7, 155.7, 154.9, 151.0, 150.7, 134.3, 134.0, 131.4, 129.9, 129.7, 126.7, 126.2, 125.8, 125.7, 122.4, 119.9, 119.7, 111.3, 110.6, 110.5, 94.9, 93.7, 80.4, 79.6, 53.0, 52.7, 52.6, 45.6, 35.8, 35.7; **HRMS** calcd. for $C_{21}H_{21}N_2O_6^+$ $[M + H]^+$ 397.1394, found 397.1383.

Methyl 3a-((4-chlorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2k)

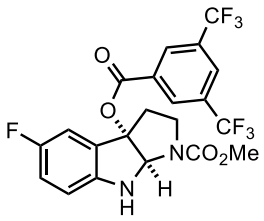


Following the **general procedure G**, *N*-hydroxyindole **1a** (88.0 mg, 0.376 mmol) afforded an inseparable mixture of pyrroloindoline **2k-Int** and indolyl *N*-carboxylate **2k** (109 mg, 7.7:1, overall 78%) as a pale yellow oil after

purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3). When following the **general procedure H** for 16 h, *N*-hydroxyindole **1a** (70.9 mg, 0.303 mmol) afforded pyrroloindoline **2k** (68.8 mg, 61%) as a sole product.

***R*$_f$**=0.53 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.61 and 7.54 (d, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.80 (q, *J* = 6.9 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 5.75 (s, 1H), 3.93 and 3.81 (t, *J* = 9.8 Hz, 1H), 3.79 and 3.72 (s, 3H), 3.25 – 3.19 (m, 1H), 3.06 and 2.96 (dd, *J* = 13.0, 6.3 Hz, 0H), 2.73 – 2.65 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 164.6, 155.7, 154.9, 151.0, 150.8, 139.8, 139.8, 131.3, 128.8, 128.7, 128.0, 128.0, 126.7, 126.1, 125.9, 125.7, 119.8, 119.5, 110.5, 110.3, 94.7, 93.5, 80.4, 79.6, 52.9, 52.7, 45.6, 45.6, 35.8, 35.7; **HRMS** calcd. for $C_{19}H_{18}ClN_2O_4^+$ $[M + H]^+$ 373.0950, found 373.0947.

Methyl 3a-((3,5-bis(trifluoromethyl)benzoyl)oxy)-5-fluoro-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2l)

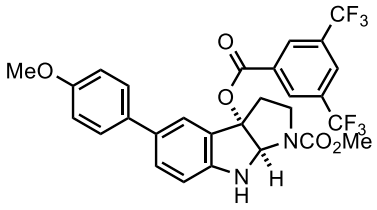


Following the **general procedure H** for 8 h, *N*-hydroxyindole **1f** (43.0 mg, 0.170 mmol) afforded pyrroloindoline **2l** (52.8 mg, 63%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R*$_f$**=0.57 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 55:45 mixture of rotamers): δ 8.42 (s, 2H), 8.06 (s, 1H), 7.35 and 7.31 (d, *J* = 8.2 Hz, 1H), 6.94 (t, *J* = 8.8 Hz, 1H), 6.64 and 6.62 (d, *J* = 4.2 Hz, 1H), 5.80 and 5.78 (s, 1H), 5.19 and 4.83 (s, 1H), 3.97 and 3.85 (t, *J* = 9.9 Hz, 1H), 3.81 and 3.74 (s, 3H), 3.29 – 3.21 (m, 1H), 3.11 – 3.01 (m, 1H), 2.73 – 2.65 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 162.8, 157.2 (d, *J* = 237.3 Hz), 157.1 (d, *J* = 237.0 Hz), 155.6, 154.7, 147.3, 147.1, 132.4 (q, *J* = 34.1 Hz), 132.2, 130.0 (d, *J* = 3.9 Hz), 126.8, 126.1 (br t, *J* = 9.4 Hz), 122.9 (q, *J* = 273.1 Hz), 118.4 (d, *J* = 24.0 Hz), 113.8 (d, *J* = 24.9 Hz), 113.5 (d, *J* = 24.6 Hz), 111.3 (d, *J* = 8.1 Hz), 111.2 (d, *J* = 7.8 Hz), 113.3, 111.4, 111.3, 111.2, 95.5, 94.3, 81.1, 80.4, 53.1, 52.8, 45.6, 45.6, 35.7, 31.0; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −63.0, −124.1 (q, *J* = 4.5 Hz), −124.5 (q, *J* = 4.5 Hz);

HRMS calcd. for $C_{21}H_{16}F_7N_2O_4^+$ $[M + H]^+$ 493.0993, found 493.0990.

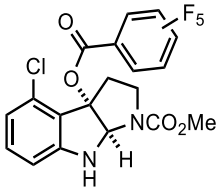
Methyl 3a-((3,5-bis(trifluoromethyl)benzoyl)oxy)-5-(4-methoxyphenyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2m)



Following the **general procedure F**, *N*-hydroxyindole **1e** (51.0 mg, 0.150 mmol) afforded pyrroloindoline **2m** (47.8 mg, 55%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

***R**f*=0.43 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.56 and 8.44 (s, 2H), 8.11 and 8.05 (s, 1H), 7.83 and 7.78 (s, 1H), 7.47 – 7.43 (m, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.3 Hz, 1H), 5.86 and 5.83 (s, 1H), 4.00 and 3.88 (t, *J* = 8.2 Hz, 1H), 3.84 and 3.77 (s, 3H), 3.34 – 3.26 (m, 1H), 3.20 and 3.14 (dd, *J* = 12.7, 6.0 Hz, 1H), 2.79 – 2.70 (m, 1H) ; **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.9, 162.9, 158.8, 158.8, 155.8, 154.9, 150.2, 149.9, 133.7, 133.6, 133.2, 132.9, 132.8, 132.4, 132.4 (q, *J* = 34.0 Hz), 132.3 (q, *J* = 34.0 Hz), 130.4, 130.3, 130.2, 130.1, 130.0, 127.7, 126.7, 126.7, 127.1 – 126.8 (m), 126.3, 125.7, 125.6, 125.0, 124.6, 123.0 (q, *J* = 273.1 Hz), 122.91 (q, *J* = 273.1 Hz), 115.1, 114.3, 110.9, 110.7, 95.8, 94.6, 80.7, 80.0, 55.5, 53.2, 52.9, 45.7, 35.8, 35.8; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –62.9, –63.0; **HRMS** calcd. for $C_{28}H_{23}F_6N_2O_5^+$ $[M + H]^+$ 581.1506, found 581.1499.

Methyl 4-chloro-3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2n)

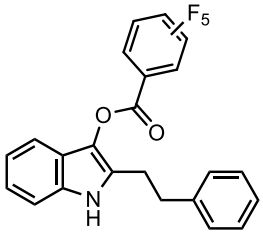


Following the **general procedure F**, *N*-hydroxyindole **1l** (75.0 mg, 0.279 mmol) afforded pyrroloindoline **2n**

(58.1 mg, 45%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

***R*$_f$**=0.57 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.13 (t, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 5.97 and 5.91 (s, 1H), 5.30 (s, 1H), 3.92 – 3.87 and 3.83 – 3.79 (m, 1H), 3.79 and 3.75 (s, 3H), 3.32 (q, *J* = 9.7 Hz, 1H), 2.88 – 2.72 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 157.7, 157.6, 155.8, 154.9, 152.2, 152.1, 145.9 (dm, *J* = 257.6 Hz), 143.6 (dm, *J* = 259.0 Hz), 137.8 (ddd, *J* = 256.1, 18.2, 12.4, 5.3 Hz), 132.5, 130.4, 121.9, 120.3, 120.0, 108.7, 108.6, 107.7 (t, *J* = 14.2 Hz), 96.7, 95.6, 79.8, 79.2, 53.0, 52.9, 44.3, 44.2, 35.8, 35.4; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −137.1 (tt, *J* = 20.3, 6.0 Hz), −147.5 (t, *J* = 20.7 Hz), −147.8 (t, *J* = 20.7 Hz), −160.2 (dtd, *J* = 32.6, 20.2, 6.2 Hz); **HRMS** calcd. for $C_{19}H_{13}ClF_5N_2O_4^+$ $[M + H]^+$ 463.0479, found 463.0475.

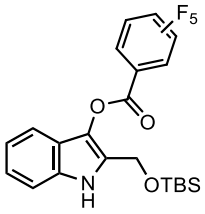
2-Phenethyl-1H-indol-3-yl 2,3,4,5,6-pentafluorobenzoate (2o)



Following the **general procedure H** for 16 h, *N*-hydroxyindole **1p** (30.0 mg, 0.126 mmol) afforded indole **2o** (32.1 mg, 59%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5).

***R*$_f$**=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.59 (br s, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.29 – 7.15 (m, 6H), 3.11 – 2.98 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.6, 145.7 (dm, *J* = 258.2 Hz), 143.6 (dm, *J* = 255.2 Hz), 140.8, 138.0 (dm, *J* = 255.8 Hz), 132.8, 128.8, 128.5, 127.9, 126.6, 126.1, 122.4, 120.8, 120.5, 117.0, 111.2, 107.9 (td, *J* = 16.2, 4.1 Hz), 35.1, 27.1; **^{19}F NMR** (471 MHz, $CDCl_3$): δ −137.3 (dp, *J* = 16.9, 5.8 Hz), −147.6 (tt, *J* = 20.9, 4.8 Hz), −159.7 – −159.8 (m); **HRMS** calcd. for $C_{23}H_{15}F_5NO_2^+$ $[M + H]^+$ 432.1018, found 432.1021.

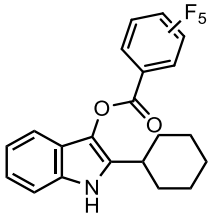
2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-1H-indol-3-yl 2,3,4,5,6-pentafluorobenzoate (2p)



Following the **general procedure H for** 16 h, *N*-hydroxyindole **1q** (51.1 mg, 0.184 mmol) afforded indole **2p** (52.9 mg, 61%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5).

***R**f*=0.45 (silica gel, hexanes:EtOAc = 8:2); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.20 (br s, 1H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 4.87 (s, 2H), 0.94 (s, 9H), 0.12 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.2, 145.8 (dm, *J* = 244.4 Hz), 143.8 (dm, *J* = 261.0 Hz), 138.0 (dm, *J* = 256.0 Hz), 132.9, 127.0, 124.5, 122.8, 120.8, 120.6, 117.5, 111.6, 56.5, 26.0, −5.3; **^{19}F NMR** (471MHz, $CDCl_3$): δ −137.2 (dp, *J* = 17.2, 6.0 Hz), −147.4 (tt, *J* = 20.9, 4.6 Hz), −159.6 – −159.8 (m); **HRMS** calcd. for $C_{22}H_{23}F_5NO_3Si^+$ $[M + H]^+$ 472.1362, found 472.1365.

2-Cyclohexyl-1H-indol-3-yl 2,3,4,5,6-pentafluorobenzoate (2q)



Following the **general procedure H** for 16 h, *N*-hydroxyindole **1r** (28.8 mg, 0.134 mmol) afforded indole **2q** (43.3 mg, 76%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5).

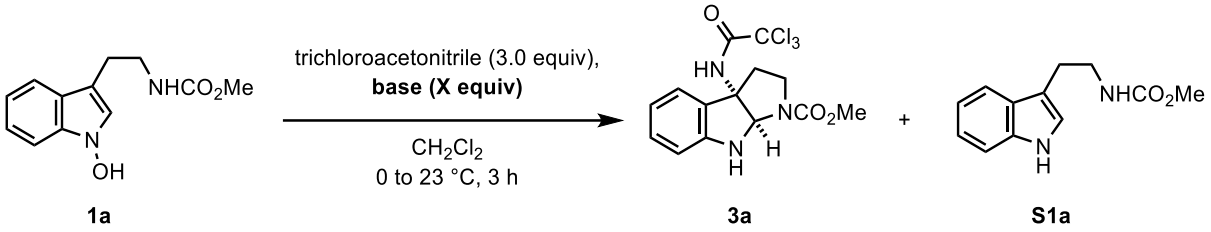
***R**f*=0.45 (silica gel, hexanes:EtOAc = 8:2); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 2.85 (tt, *J* = 12.0, 3.5 Hz, 1H), 2.02 (dd, *J* = 12.5, 3.4 Hz, 2H), 1.88 (dt, *J* = 13.1, 3.3 Hz, 2H), 1.79 (dt, *J* = 13.1, 3.4 Hz, 1H), 1.54 – 1.37 (m, 4H), 1.29 (ddt, *J* = 12.3, 8.0, 3.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.8, 145.6 (dm, *J* = 257.0 Hz), 143.6 (d, *J* = 252.5 Hz), 138.0 (dddd, *J* = 250.9, 15.8, 12.6, 4.8 Hz), 133.1, 132.6, 124.8, 122.2, 121.0, 120.4, 116.9, 111.3,

108.2 (t, J = 16.7 Hz), 35.3, 32.2, 26.5, 26.0; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −137.5 (dp, J = 16.9, 5.5, 5.1 Hz), −148.0 (tt, J = 21.1, 4.8 Hz), −159.7 – −159.9 (m); **HRMS** calcd. for $C_{21}H_{17}F_5NO_2^+$ $[M + H]^+$ 410.1174, found 410.1176.

5. C–N Bond Formation via Indolyl 1,3-Heteroatom Transposition (IHT)

5.1. Optimization of the C3-Amidation Reaction Conditions

Table S3. Evaluation of bases.[a]

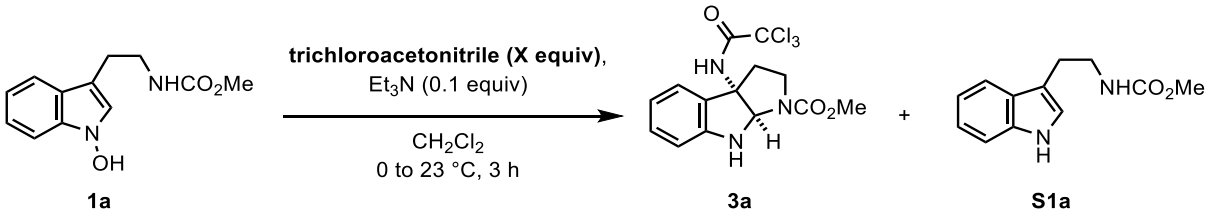


1a **3a** **S1a**

entry	base	equiv	yield of 3a (%)[b]	yield of S1a (%)[b]
1	DIPEA	0.1	51%	7%
2	DBU	0.1	70%	5%
3	DABCO	0.1	59%	6%
4	pyridine	0.1	<5%	54%
5	NaH	1.1	68%	5%
6	**Et_3N**	**0.1**	**75% (71%)**	**<1%**
7	Et_3N	1.0	37%	21%

[a]Reactions were performed with trichloroacetonitrile (3.0 equiv) and base in CH_2Cl_2 (0.05 M) at 0 to 23 °C on 0.3–1.2 mmol scale. [b]Determined by ^1H NMR analysis of the crude mixture using TCE as an internal standard and the yield of the isolated product was given in the parentheses.

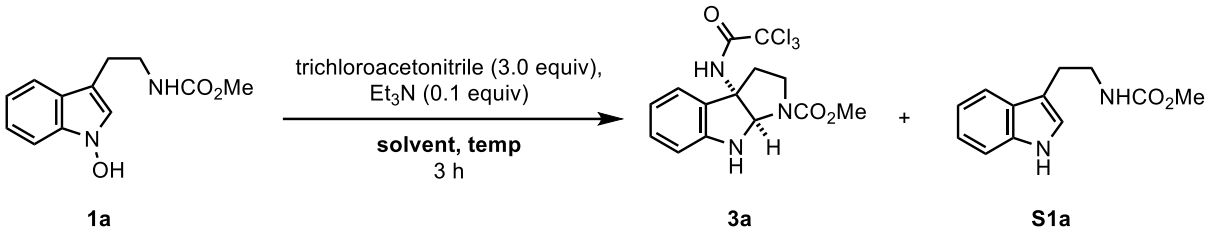
Table S4. Optimization of the stoichiometry of trichloroacetonitrile.[a]



entry	equiv	yield of 3a (%)[b]	yield of S1a (%)[b]
1	1.0	36%	22%
2	2.0	55%	9%
3	**3.0**	**79% (78%)**	**<1%**
4	4.0	48%	11%

[a]Reactions performed with trichloroacetonitrile and Et_3N (0.1 equiv) in CH_2Cl_2 (0.05 M) at 0 to 23 °C on 0.3–1.2 mmol scale. [b]Determined by ^1H NMR analysis of the crude mixture using TCE as an internal standard and the yield of the isolated product was given in the parentheses.

Table S5. Evaluation of solvents and temperatures.[a]

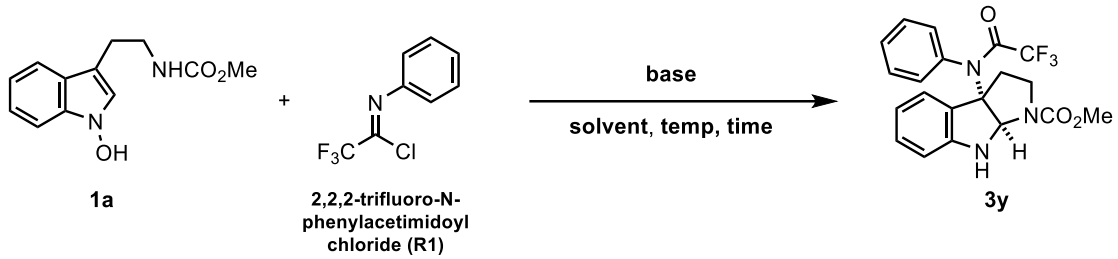


1a **3a** **S1a**

entry	solvent	temperature	time	yield of 3a (%)[b]	yield of S1a (%)[b]
1	THF	0 to 23 °C	3 h	4%	48%
2	toluene	0 to 23 °C	3 h	11%	63%
3	MeCN	0 to 23 °C	3 h	16%	72%
4	DMF	0 to 23 °C	3 h	<5%	56%
5	**CH_2Cl_2**	**0 to 23 °C**	**3 h**	**75% (73%)**	**<1%**
6	CH_2Cl_2	23 °C	3 h	67%	<1%
7	CH_2Cl_2	0 °C	24 h	38%	33%

[a]Reactions performed with trichloroacetonitrile (3.0 equiv) and Et_3N (0.1 equiv) in solvent (0.05 M) at indicated temperature on 0.3–1.2 mmol scale. [b]Determined by ^1H NMR analysis of the crude mixture using TCE as an internal standard and the yield of the isolated product was given in the parentheses.

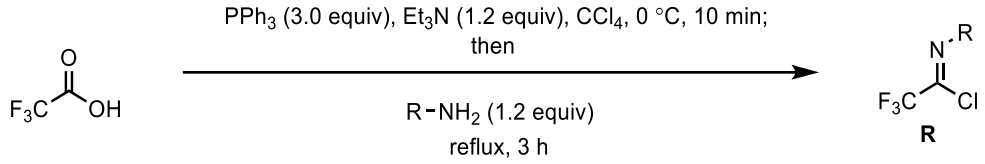
Table S6. Evaluation of reaction conditions using trifluoroacetimidoyl chloride.[a]



entry	base (equiv)	equiv of R1	solvent	temperature	time	yield of 3y (%)[b]
1	Et_3N (1.1 equiv)	1.5	THF	0 °C	1 h	8%
2	LDA (1.1 equiv)	1.5	THF	0 °C	1 h	13%
3	LiHMDS (1.1 equiv)	1.5	THF	0 °C	1 h	17%
4	NaHMDS (1.1 equiv)	1.5	THF	0 °C	1 h	16%
5	**NaH (1.1 equiv)**	**1.5**	**THF**	**0 °C**	**1 h**	**34% (28%)**
6	NaH (1.1 equiv)	1.5	CH_2Cl_2	0 °C	1 h	26% (20%)
7	NaH (2.0 equiv)	1.5	THF	0 °C	1 h	24%
8	NaH (1.1 equiv)	3.0	THF	0 °C	1 h	21%
9	NaH (1.1 equiv)	1.5	THF	–20 °C	12 h	11%
10	NaH (1.1 equiv)	1.5	THF	–78 °C	24 h	19%

[a]Reactions performed with imidoyl chloride and base in solvent (0.05 M) at indicated temperature on 0.3–1.2 mmol scale. [b] Determined by ^1H NMR analysis of the crude mixture using TCE as an internal standard and the yield of the isolated product was given in the parentheses.

5.2. Preparation of Trifluoroacetimidoyl Chlorides



Trifluoroacetimidoyl chlorides were prepared according to the literature procedure.[17] To an oven-dried round-bottom flask equipped with a stir bar, septum, and condenser were added TFA (1.0 equiv), PPh_3 (3.0 equiv), Et_3N (1.2 equiv), and CCl_4 (5.0 equiv) at 23 °C. The resulting solution was cooled to 0 °C and stirred for 10 min before the solution of amine (1.2 equiv) in CCl_4 (5.0 equiv) was added. The reaction mixture was heated to reflux in a pre-heated oil bath and stirred for 2 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The crude product was re-dissolved in hexanes and filtered, and the filter cake was washed with hexanes three times. The resulting filtrate was concentrated under reduced pressure, and the crude product was distilled to afford the imidoyl chloride **R**.

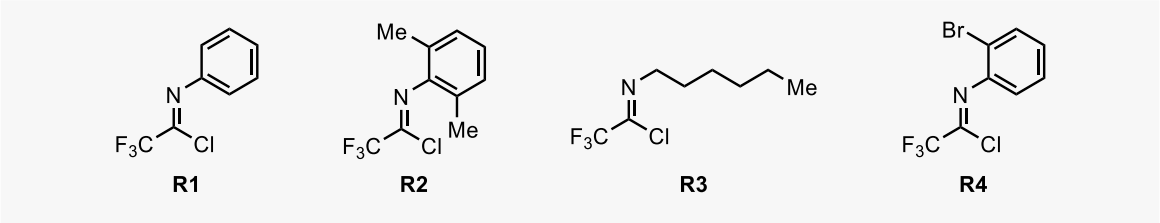


Figure S7. List of trifluoroacetimidoyl chlorides.

The spectral data matched to those reported in the literature: 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (**R1**)[17], *N*-(2,6-dimethylphenyl)-2,2,2-trifluoroacetimidoyl chloride (**R2**)[15], 2,2,2-trifluoro-*N*-hexylacetimidoyl chloride (**R3**)[15], *N*-(2-bromophenyl)-2,2,2-trifluoroacetimidoyl chloride (**R4**)[18]

5.3. General Procedure for C3-Amidation of Indole Derivatives (Scheme 3)

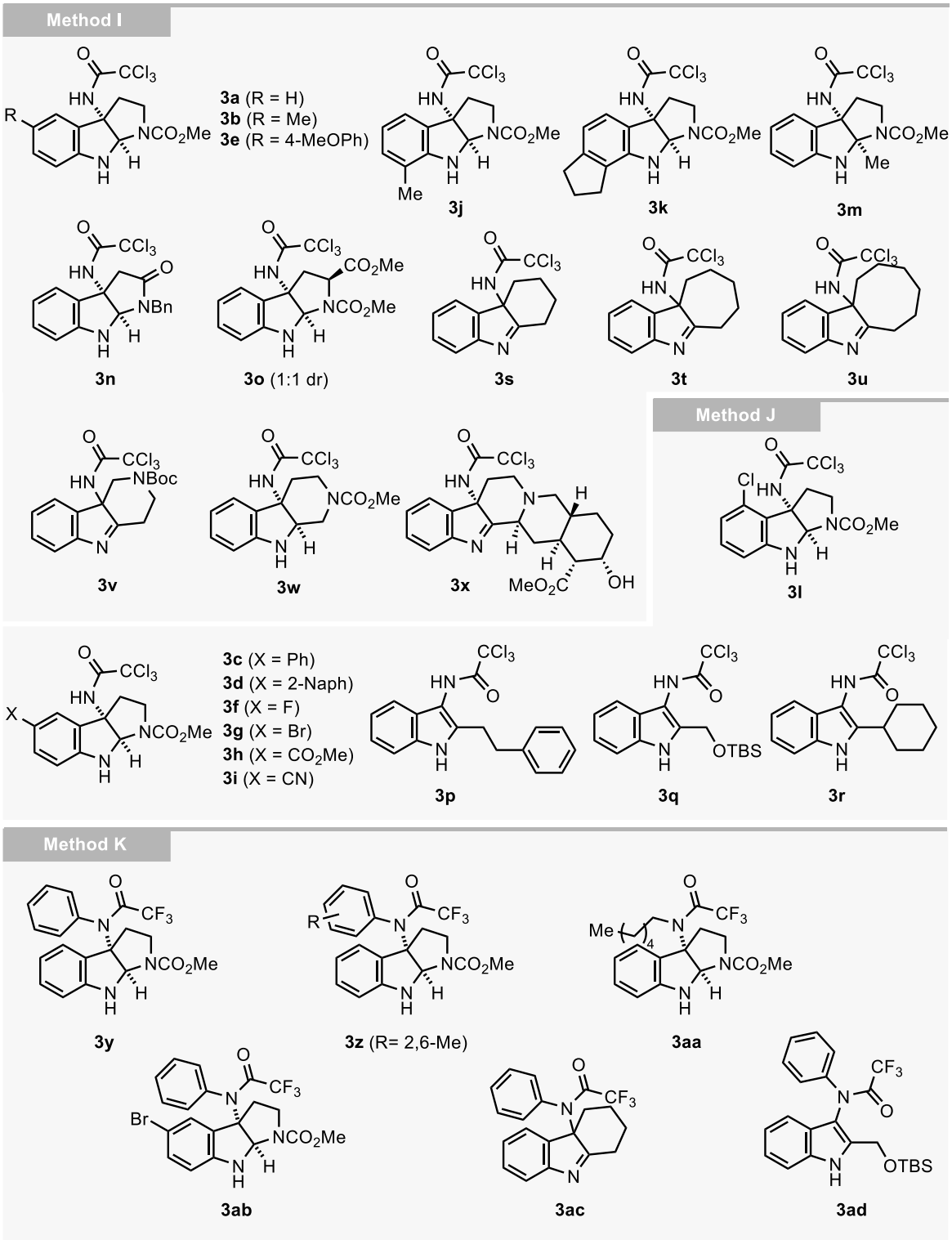
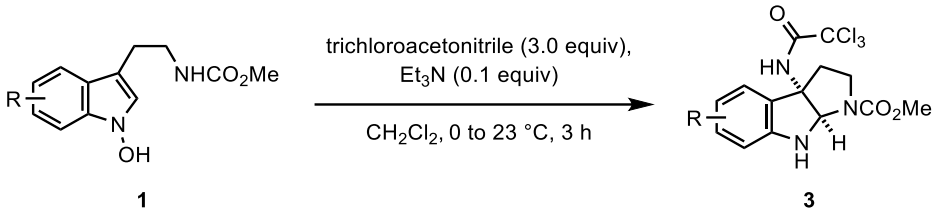


Figure S8. List of C3-amidated products categorized by methods of C3-amidation.

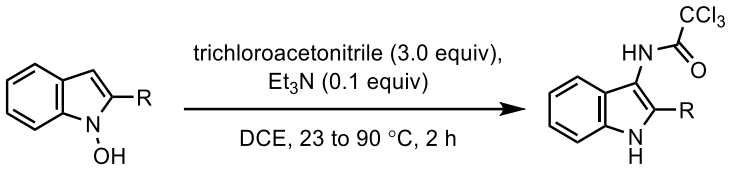
General procedure I



1 **3**

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1** (1.0 equiv) and CH_2Cl_2 (0.05 M in **1**) at 23 °C. The resulting solution was cooled to 0 °C, and trichloroacetonitrile (3.0 equiv) and Et_3N (0.1 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 3 h before it was quenched with H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the desired product **3**.

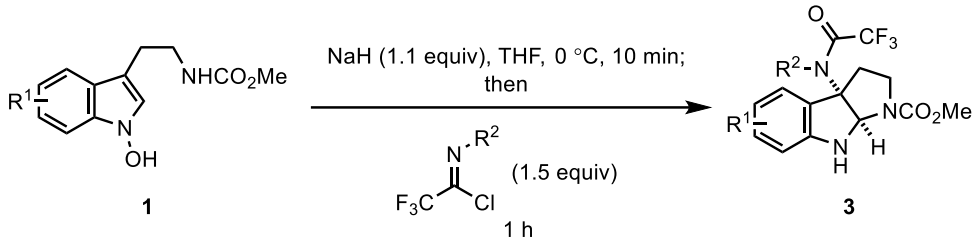
General procedure J



1 **3**

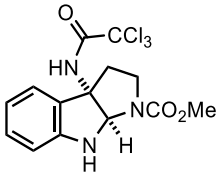
To an oven-dried heavy-wall pressure tube equipped with a stir bar and septum were successively added *N*-hydroxyindole **1** (1.0 equiv) and DCE (0.05 M in **1**) at 23 °C, followed by trichloroacetonitrile (3.0 equiv) and Et_3N (0.1 equiv). The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 2 h, before it was cooled to 23 °C and quenched with H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the desired product **3**.

General procedure K



To an oven-dried round-bottom flask equipped with a stir bar and septum were successively added *N*-hydroxyindole **1** (1.0 equiv) and THF (0.05 M in **1**) at 23 °C. The resulting solution was cooled to 0 °C, and NaH (60% in mineral oil, 1.1 equiv) was added to the solution. The reaction mixture was stirred for 10 min, then imidoyl chloride (1.5 equiv) was added. The resulting mixture was stirred for additional 1 h at 0 °C before it was quenched with brine. The layers were separated and the aqueous layer was extracted with EtOAc three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the desired product **3**.

Methyl 3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3a)

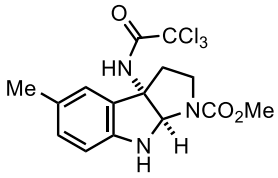


Following the **general procedure I**, *N*-hydroxyindole **1a** (133 mg, 0.568 mmol) afforded pyrroloindoline **3a** (168 mg, 78%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.51 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.34 and 7.30 (d, *J* = 7.5 Hz, 1H), 7.23 – 7.19 (m, 1H), 6.88 – 6.80 (m, 2H), 6.68 (d, *J* = 7.3 Hz, 1H), 5.70 and 5.68 (s, 1H), 3.88 and 3.78 (t, *J* = 9.9 Hz, 1H), 3.77 and 3.70 (s, 3H), 3.16 – 3.08 (m, 1H), 3.01 – 2.91 (m, 1H), 2.50 and 2.41 (dd, *J* = 12.5, 6.5 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 161.0, 155.5, 154.6, 149.9, 149.7, 131.1, 131.1, 127.0,

126.8, 123.8, 123.5, 120.0, 119.8, 110.5, 110.4, 92.3, 78.3, 78.2, 72.0, 70.9, 52.9, 52.6, 45.4, 45.3, 33.0; **HRMS** calcd. for $C_{14}H_{15}Cl_3N_3O_3^+$ $[M + H]^+$ 378.0174, found 378.0173.

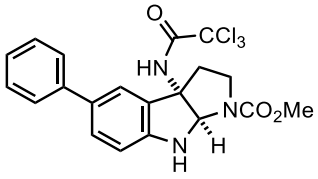
Methyl 5-methyl-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3b)



Following the **general procedure I,** *N*-hydroxyindole **1b** (72.0 mg, 0.290 mmol) afforded pyrroloindoline **3b** (77.2 mg, 68%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R*$_f$**=0.56 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 55:45 mixture of rotamers): δ 7.14 and 7.10 (s, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.80 and 6.76 (s, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.69 and 5.67 (s, 1H), 3.89 and 3.77 (t, *J* = 9.7 Hz, 1H), 3.77 and 3.70 (s, 3H), 3.12 (tt, *J* = 10.9, 6.8 Hz, 1H), 3.01 – 2.91 (m, 1H), 2.47 and 2.39 (dd, *J* = 12.4, 6.1 Hz, 1H), 2.30 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 161.0, 155.6, 154.7, 147.7, 147.5, 131.8, 131.7, 129.7, 129.5, 127.2, 127.0, 124.2, 123.9, 110.7, 110.5, 92.3, 78.5, 72.1, 71.0, 52.9, 52.6, 45.5, 45.3, 32.7, 32.6, 21.0; **HRMS** calcd. for $C_{15}H_{17}Cl_3N_3O_3^+$ $[M + H]^+$ 392.0330, found 392.0330.

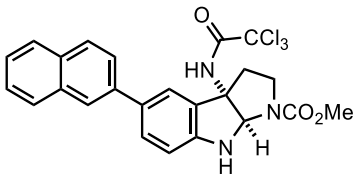
Methyl 5-phenyl-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3c)



Following the **general procedure J,** *N*-hydroxyindole **1c** (35.6 mg, 0.115 mmol) afforded pyrroloindoline **3c** (26.1 mg, 50%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.44 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.57 and 7.52 (s, 1H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 6.87 and 6.84 (s, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 5.76 and 5.74 (s, 1H), 3.94 and 3.83 (t, *J* = 9.6 Hz, 1H), 3.80 and 3.72 (s, 3H), 3.20 (tt, *J* = 11.0, 5.6 Hz, 1H), 3.00 (dq, *J* = 21.9, 10.9 Hz, 1H), 2.57 and 2.49 (dd, *J* = 12.5, 6.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.2, 155.6, 154.7, 149.3, 149.2, 140.9, 140.8, 133.7, 133.5, 130.3, 130.2, 129.0, 127.9, 127.7, 126.9, 126.7, 122.5, 122.2, 110.9, 110.7, 92.3, 78.7, 72.1, 71.0, 53.0, 52.7, 45.5, 45.4, 33.0; **HRMS** calcd. for $C_{20}H_{19}Cl_3N_3O_3^+$ $[M + H]^+$ 454.0487, found 454.0487.

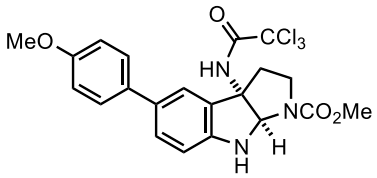
Methyl 5-(naphthalen-2-yl)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3d)



Following the **general procedure J**, *N*-hydroxyindole **1d** (47.2 mg, 0.131 mmol) afforded pyrroloindoline **3d** (29.7 mg, 45%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.41 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, MeOD, 60:40 mixture of rotamers): δ 7.98 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.76 – 7.70 (m, 2H), 7.58 (d, *J* = 8.3 Hz, 1H), 7.44 (dt, *J* = 19.7, 7.1 Hz, 2H), 6.78 (d, *J* = 8.2 Hz, 1H), 5.84 and 5.83 (s, 1H), 3.83 (t, *J* = 10.3 Hz, 1H).3.80 and 3.74 (s, 3H), 3.22 (td, *J* = 10.9, 10.4, 6.9 Hz, 1H), 2.80 – 2.60 (m, 2H); **^{13}C NMR** (126 MHz, MeOD): δ 163.5, 157.2, 156.9, 151.4, 140.0, 135.4, 133.7, 133.5, 133.4, 130.4, 130.0, 129.9, 129.3, 129.0, 128.6, 127.2, 126.5, 126.2, 125.3, 123.7, 123.6, 111.3, 111.1, 93.9, 81.2, 80.7, 73.8, 72.8, 53.4, 53.2, 46.1, 46.0, 37.0, 36.6; **HRMS** calcd. for $C_{24}H_{21}Cl_3N_3O_3^+$ $[M + H]^+$ 504.0643, found 504.0648.

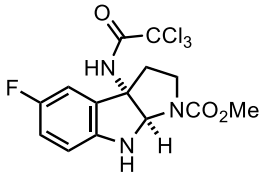
Methyl 5-(4-methoxyphenyl)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3e)



Following the **general procedure I,** *N*-hydroxyindole **1e** (40.0 mg, 0.118 mmol) afforded pyrroloindoline **3e** (37.6 mg, 68%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.52 (s, 1H), 7.48 – 7.40 (m, 4H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.87 and 6.84 (s, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 5.75 and 5.73 (s, 1H), 3.92 and 3.86 (t, *J* = 8.8 Hz, 1H), 3.84 (s, 3H), 3.79 and 3.72 (s, 3H), 3.20 (td, *J* = 10.2, 5.5 Hz, 1H), 3.00 (tt, *J* = 19.2, 9.8 Hz, 1H), 2.56 and 2.48 (dd, *J* = 12.4, 6.4 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 161.1, 158.9, 155.6, 154.7, 148.9, 148.7, 133.5, 133.5, 133.4, 133.2, 129.8, 129.8, 128.4, 127.8, 127.7, 122.0, 121.8, 114.4, 110.9, 110.7, 92.3, 78.6, 72.1, 71.0, 55.5, 53.0, 52.7, 45.5, 45.4, 33.0; **HRMS** calcd. for $C_{21}H_{21}Cl_3N_3O_4^+$ [M + H]$^+$ 484.0592, found 484.0595.

Methyl 5-fluoro-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3f)

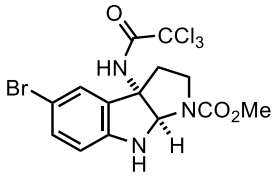


Following the **general procedure J,** *N*-hydroxyindole **1f** (68.4 mg, 0.271 mmol) afforded pyrroloindoline **3f** (55.9 mg, 52%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

***R**f*=0.30 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.09 and 7.04 (dd, *J* = 7.9, 2.6 Hz, 1H), 6.94 – 6.85 (m, 2H), 6.62 (dd, *J* = 8.9, 4.2 Hz, 1H), 5.69 and 5.66 (s, 1H), 3.89 and 3.79 (t, *J* = 9.7 Hz, 1H), 3.77 and 3.70 (s, 3H), 3.16 (td, *J* = 10.7, 6.4 Hz, 1H), 2.93 – 2.80 (m, 1H), 2.55 and 2.45

(dd, J = 12.7, 6.5 Hz,1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.2, 160.2, 157.4 (d, J = 238.1 Hz), 157.3 (d, J = 238.1 Hz), 157.2, 155.5, 154.7, 146.0, 145.9, 128.2 (d, J = 7.6 Hz), 128.1 (d, J = 7.5 Hz), 117.7 (d, J = 22.5 Hz), 117.6 (d, J = 22.5 Hz), 111.3, 111.2 (d, J = 24.2 Hz), 110.8 (d, J = 24.2 Hz), 92.2, 79.6, 78.6, 72.1, 71.0, 53.0, 52.7, 45.4, 45.3, 33.6, 33.5; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −123.6 (q, J = 8.1 Hz), −123.9 (td, J = 8.5, 4.1 Hz); **HRMS** calcd. for $C_{14}H_{14}Cl_3FN_3O_3^+$ $[M + H]^+$ 396.0079, found 396.0081.

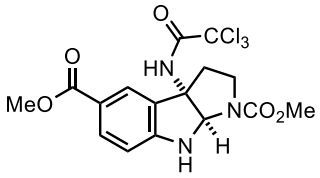
Methyl 5-bromo-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3g)



Following the **general procedure J,** *N*-hydroxyindole **1g** (63.1 mg, 0.201 mmol) afforded pyrroloindoline **3g** (58.0 mg, 63%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

***R*$_f$**=0.35 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.45 and 7.40 (s, 1H), 7.31 (d, J = 6.2 Hz, 1H), 6.82 and 6.80 (s, 1H), 6.57 (d, J = 8.3 Hz, 1H), 5.70 and 5.67 (s, 1H), 5.29 and 4.88 (s, 1H), 3.90 and 3.80 (t, J = 9.6 Hz, 1H), 3.78 and 3.71 (s, 3H), 3.16 (td, J = 10.8, 6.5 Hz, 1H), 2.91 (ddd, J = 24.2, 13.1, 9.3 Hz, 1H), 2.50 and 2.42 (dd, J = 13.0, 6.4 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 161.2, 155.6, 154.6, 149.0, 134.0, 129.2, 129.0, 126.9, 126.7, 112.1, 111.9, 111.1, 92.2, 78.9, 78.0, 71.9, 70.7, 53.1, 52.8, 45.4, 45.3, 33.5, 33.4; **HRMS** calcd. for $C_{14}H_{14}BrCl_3N_3O_3^+$ $[M + H]^+$ 455.9279, found 455.9282.

Dimethyl 3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,5(2H)-dicarboxylate (3h)

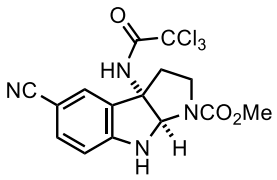


Following the **general procedure J**, *N*-hydroxyindole **1h** (32.9 mg, 0.113 mmol) afforded pyrroloindoline **3h**

(25.1 mg, 51%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

***R*$_f$**=0.30 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.00 and 7.98 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 6.76 (s, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 5.80 and 5.79 (s, 1H), 3.92 and 3.81 (t, *J* = 9.8 Hz, 1H), 3.88 (s, 3H), 3.79 and 3.72 (s, 3H), 3.15 (td, *J* = 10.6, 7.0 Hz, 1H), 30.4 – 2.90 (m, 1H), 2.48 and 2.43 (dd, *J* = 12.8, 6.9 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 166.8, 161.1, 155.6, 154.5, 153.8, 153.6, 134.0, 126.9, 126.7, 125.8, 125.6, 121.6, 121.3, 109.2, 109.0, 92.2, 78.3, 71.5, 70.4, 53.1, 52.8, 52.1, 45.3, 45.2, 33.4, 33.4; **HRMS** calcd. for $C_{16}H_{17}Cl_3N_3O_5^+$ $[M + H]^+$ 436.0228, found 436.0227.

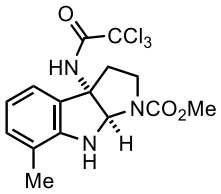
Methyl 5-cyano-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3i)



Following the **general procedure J**, *N*-hydroxyindole **1i** (30.1 mg, 0.116 mmol) afforded pyrroloindoline **3i** (25.8 mg, 55%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

***R*$_f$**=0.22 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.61 and 7.55 (s, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 6.92 (s, 1H), 6.67 (d, *J* = 8.3 Hz, 1H), 5.78 and 5.75 (s, 1H), 3.93 and 3.83 (t, *J* = 9.8 Hz, 1H), 3.79 and 3.73 (s, 3H), 3.19 (td, *J* = 10.6, 6.5 Hz, 1H), 2.89 – 2.75 (m, 1H), 2.56 and 2.47 (dd, *J* = 12.9, 6.4 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.3, 155.6, 154.4, 153.1, 153.0, 136.0, 128.1, 127.9, 127.8, 119.6, 109.9, 109.7, 102.0, 101.7, 92.1, 79.2, 78.4, 71.5, 70.3, 53.2, 52.9, 45.1, 34.9, 34.7; **HRMS** calcd. for $C_{15}H_{14}Cl_3N_4O_3^+$ $[M + H]^+$ 403.0126, found 403.0125.

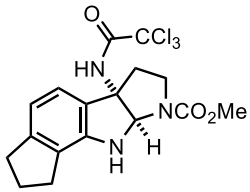
Methyl 7-methyl-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3j)



Following the **general procedure I**, *N*-hydroxyindole **1j** (57.0 mg, 0.230 mmol) afforded pyrroloindoline **3j** (42.3 mg, 47%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

R_f=0.44 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.18 and 7.14 (d, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.81 – 6.76 (m, 2H), 5.75 and 5.73 (s, 1H), 5.09 and 4.64 (s, 1H), 3.89 and 3.79 (t, *J* = 9.6 Hz, 1H), 3.79 and 3.71 (s, 3H), 3.13 (qd, *J* = 10.7, 6.3 Hz, 1H), 3.03 – 2.91 (m, 1H), 2.46 and 2.38 (dd, *J* = 12.2, 6.1 Hz, 1H), 2.16 and 2.15 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 161.0, 155.6, 154.8, 148.6, 148.5, 132.0, 131.9, 126.4, 126.1, 121.0, 120.8, 120.3, 120.1, 120.0, 119.9, 92.3, 78.1, 72.5, 71.4, 53.0, 52.6, 45.5, 45.3, 33.0, 32.9, 16.8; **HRMS** calcd. for $C_{15}H_{17}Cl_3N_3O_3^+$ $[M + H]^+$ 392.0330, found 392.0330.

Methyl 5b-(2,2,2-trichloroacetamido)-1,2,3,5b,6,7,8a,9-octahydro-8H-cyclopenta[g]pyrrolo[2,3-b]indole-8-carboxylate (3k)

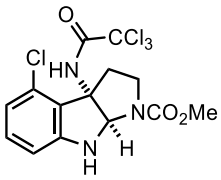


Following the **general procedure I**, *N*-hydroxyindole **1k** (41.0 mg, 0.149 mmol) afforded pyrroloindoline **3k** (34.4 mg, 55%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

R_f=0.48 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.12 and 7.09 (d, *J* = 7.6 Hz, 1H), 6.77 – 6.74 (m, 2H), 5.75 and 5.74 (s, 1H), 5.06 and 4.60 (s, 1H), 3.89 and 3.79 (t, *J* = 9.6 Hz, 1H), 3.79 and 3.71 (s, 3H), 3.19 – 3.09 (m, 1H), 3.00 (dtd, *J* = 20.0, 11.6, 8.6 Hz, 1H), 2.88 (m, 2H), 2.72 (m, 2H), 2.43 and 2.36 (dd, *J* = 12.1, 6.6 Hz, 1H), 2.11 (h, *J* = 7.4 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.0,

160.9, 155.6, 154.8, 148.5, 146.1, 145.9, 125.8, 125.6, 124.7, 124.5, 121.4, 121.2, 116.2, 115.9, 92.4, 78.6, 72.3, 71.2, 53.0, 52.6, 45.5, 45.4, 33.1, 32.9, 32.8, 29.5, 25.5, 25.4; **HRMS** calcd. for $C_{17}H_{19}Cl_3N_3O_3^+$ $[M + H]^+$ 418.0487, found 418.0494.

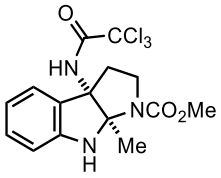
Methyl 4-chloro-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3l)



Following the **general procedure J**, *N*-hydroxyindole **1l** (31.7 mg, 0.118 mmol) afforded pyrroloindoline **3l** (27.8 mg, 57%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

***R**f*=0.41 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.12 (t, *J* = 8.0 Hz, 1H), 1.12 and 7.07 (s, 1H), 6.74 (dd, *J* = 7.9, 3.6 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 5.87 and 5.86 (s, 1H), 5.35 and 4.99 (s, 1H), 3.95 – 3.91 and 3.86 – 3.82 (m, 1H), 3.78 and 3.73 (s, 3H), 3.24 (q, *J* = 8.4 Hz, 1H), 2.80 (dd, *J* = 8.6, 5.9 Hz, 1H), 2.84 – 2.78 and 2.71 – 2.65 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.0, 160.8, 155.7, 154.7, 151.9, 151.8, 132.3, 130.3, 130.2, 122.9, 122.6, 120.2, 119.9, 108.7, 108.5, 92.4, 78.5, 77.9, 73.0, 71.8, 53.0, 52.8, 44.8, 33.8, 31.1; **HRMS** calcd. for $C_{14}H_{14}Cl_4N_3O_3^+$ $[M + H]^+$ 411.9784, found 411.9789.

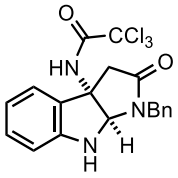
Methyl 8a-methyl-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3m)



Following the **general procedure I**, *N*-hydroxyindole **1m** (27.0 mg, 0.109 mmol) afforded pyrroloindoline **3m** (22.4 mg, 52%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.63 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.44 (d, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.84 – 6.81 (m, 2H), 6.68 (d, *J* = 7.9 Hz, 1H), 5.87 (s, 1H), 3.64 (s, 3H), 3.09 – 3.03 (m, 1H), 2.95 (dd, *J* = 12.9, 6.6 Hz, 1H), 2.85 – 2.78 (m, 1H), 1.75 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.2, 154.8, 148.9, 130.7, 128.2, 124.6, 120.2, 110.8, 87.1, 71.5, 52.3, 45.5, 30.3, 19.5; **HRMS** calcd. for $C_{15}H_{17}Cl_3N_3O_3^+$ $[M + H]^+$ 392.0330, found 392.0333.

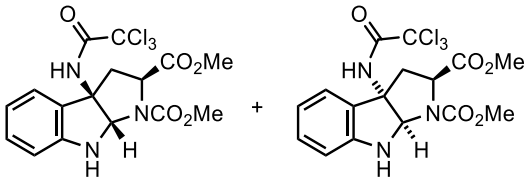
***N*-(1-Benzyl-2-oxo-2,3,8,8a-tetrahydropyrrolo[2,3-b]indol-3a(1H)-yl)-2,2,2-trichloroacetamide (3n)**



Following the **general procedure I**, *N*-hydroxyindole **1n** (95.1 mg, 0.339 mmol) afforded pyrroloindoline **3n** (87.8 mg, 61%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R**f*=0.50 (silica gel, hexanes:EtOAc = 6:4); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.39 – 7.27 (m, 6H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.76 (s, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 5.43 and 5.42 (s, 1H), 4.95 (d, *J* = 15.4 Hz, 1H), 4.38 (d, *J* = 3.7 Hz, 1H), 4.31 (d, *J* = 15.4 Hz, 1H), 3.51 (d, *J* = 16.9 Hz, 1H), 3.03 (d, *J* = 16.8 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.6, 161.1, 148.4, 135.7, 131.6, 129.7, 129.1, 128.0, 127.8, 123.9, 121.7, 112.7, 92.0, 78.7, 65.3, 43.8, 40.1; **HRMS** calcd. for $C_{19}H_{17}Cl_3N_3O_2^+$ $[M + H]^+$ 424.0381, found 424.0383.

Dimethyl (2S)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (3o)

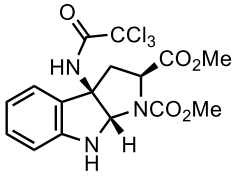


3o-1 **3o-2**

Following the **general procedure I**, *N*-hydroxyindole **1o** (108 mg, 0.369 mmol) afforded pyrroloindoline **3o** (77.4 mg, 48%, **3o-1**: **3o-2** = 1.3:1) as a pale yellow oil after purification by flash column chromatography (silica gel,

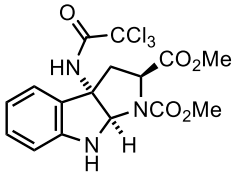
CH_2Cl_2:acetone = 1:0 → 97:3). Both diastereomers were separated by preparative thin layer chromatography (silica gel, CH_2Cl_2:acetone = 95:5) and characterized respectively.

Dimethyl (2S,3aR,8aS)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (3o-1)



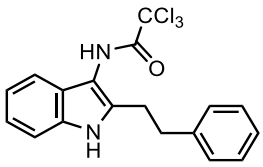
***R**f*=0.72 (silica gel, CH_2Cl_2:acetone = 95:5); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.39 and 7.30 (d, *J* = 7.5 Hz, 1H), 7.21 (q, *J* = 7.5 Hz, 1H), 7.05 and 6.93 (s, 1H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.69 (t, *J* = 8.2 Hz, 1H), 5.86 and 5.79 (s, 1H), 5.45 and 5.00 (s, 1H), 4.37 and 4.30 (dd, *J* = 8.2, 5.8 Hz, 1H), 3.81 and 3.68 (s, 3H), 3.78 (s, 3H), 3.03 and 2.77 (dd, *J* = 13.5, 6.2 Hz, 1H), 2.96 – 2.88 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 172.2, 161.2, 155.3, 154.8, 148.7, 148.3, 131.0, 130.9, 127.6, 127.4, 124.0, 123.3, 120.3, 120.2, 110.9, 110.7, 92.2, 80.9, 80.5, 71.2, 69.8, 59.5, 59.1, 53.4, 53.0, 52.9, 52.9, 38.4, 37.8; **HRMS** calcd. for $C_{16}H_{17}Cl_3N_3O_5^+$ $[M + H]^+$ 436.0228, found 436.0240.

Dimethyl (2S,3aS,8aR)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (3o-2)



***R**f*=0.70 (silica gel, CH_2Cl_2:acetone = 95:5); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.25 – 7.19 (m, 2H), 6.80 (dt, *J* = 14.9, 7.4 Hz, 1H), 6.74 – 6.65 (m, 1H), 5.77 (s, 1H), 4.75 and 4.63 (d, *J* = 9.3 Hz, 1H), 3.83 and 3.71 (s, 3H), 3.44 and 3.39 (dd, *J* = 12.8, 9.4 Hz, 1H), 3.22 and 3.21 (s, 3H), 2.79 (t, *J* = 12.1 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 171.2, 171.1, 161.2, 161.2, 155.2, 154.6, 150.8, 150.5, 131.8, 131.7, 126.0, 125.9, 124.1, 124.1, 119.9, 119.6, 110.6, 92.2, 78.3, 70.9, 69.7, 59.2, 59.0, 53.3, 53.0, 52.4, 36.2, 35.7; **HRMS** calcd. for $C_{16}H_{17}Cl_3N_3O_5^+$ $[M + H]^+$ 436.0228, found 436.0240.

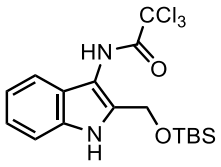
2,2,2-Trichloro-*N*-(2-phenethyl-1H-indol-3-yl)acetamide (3p)



Following the **general procedure J**, *N*-hydroxyindole **1p** (38.0 mg, 0.160 mmol) afforded indole **3p** (32.4 mg, 53%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1).

***R*$_f$**=0.27 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.78 (br s, 1H), 7.54 (s, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.29 – 7.22 (m, 3H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.14 – 7.11 (m, 3H), 3.01 (dq, *J* = 11.2, 6.0 Hz, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.5, 140.8, 134.1, 133.9, 128.9, 128.7, 126.8, 124.3, 122.5, 120.6, 117.4, 111.1, 108.7, 92.9, 35.3, 28.2; **HRMS** calcd. for $C_{18}H_{16}Cl_3N_2O^+$ $[M + H]^+$ 381.0323, found 381.0323.

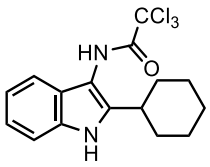
***N*-(2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-1H-indol-3-yl)-2,2,2-trichloroacetamide (3q)**



Following the **general procedure J**, *N*-hydroxyindole **1q** (89.8 mg, 0.324 mmol) afforded indole **3q** (62.8 mg, 46%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1).

***R*$_f$**=0.25 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (500 MHz, MeOD): δ 7.39 (t, *J* = 8.3 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 4.81 (s, 2H), 0.93 (s, 9H), 0.10 (s, 6H); **^{13}C NMR** (126 MHz, MeOD): δ 164.0, 136.1, 134.0, 125.1, 123.0, 120.5, 118.6, 112.5, 109.3, 79.3, 57.9, 26.4, −5.2; **HRMS** calcd. for $C_{17}H_{24}Cl_3N_2O_2Si^+$ $[M + H]^+$ 421.0667, found 421.0682.

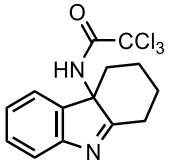
2,2,2-Trichloro-*N*-(2-cyclohexyl-1H-indol-3-yl)acetamide (3r)



Following the **general procedure J**, *N*-hydroxyindole **1r** (26.2 mg, 0.122 mmol) afforded indole **3r** (19.3 mg, 44%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1).

***R*$_f$**=0.26 (silica gel, hexanes:EtOAc = 9:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.92 (s, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 7.19 – 7.12 (m, 2H), 2.82 (tt, *J* = 11.9, 3.5 Hz, 1H), 2.04 (d, *J* = 12.4 Hz, 2H), 1.88 (dt, *J* = 12.8, 3.2 Hz, 2H), 1.79 (d, *J* = 13.2 Hz, 1H), 1.51 – 1.38 (m, 4H), 1.33 – 1.24 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.6, 139.7, 133.6, 133.5, 124.7, 123.5, 122.3, 120.9, 120.6, 118.1, 117.1, 111.5, 111.2, 106.6, 56.9, 35.9, 32.4, 32.2, 26.6, 26.1, 25.6, 16.4; **HRMS** calcd. for $C_{16}H_{18}Cl_3N_2O^+$ $[M + H]^+$ 359.0479, found 359.0480.

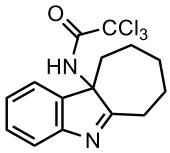
2,2,2-Trichloro-*N*-(1,2,3,4-tetrahydro-4aH-carbazol-4a-yl)acetamide (3s)



Following the **general procedure I**, *N*-hydroxyindole **1s** (126 mg, 0.673 mmol) afforded indolenine **3s** (129 mg, 58%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

***R*$_f$**=0.29 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 7.7 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 6.97 (s, 1H), 2.97 (d, *J* = 12.9 Hz, 1H), 2.70 (dd, *J* = 14.5, 2.8 Hz, 1H), 2.50 (td, *J* = 13.1, 5.7 Hz, 1H), 2.25 – 2.20 (m, 1H), 1.80 – 1.70 (m, 3H), 1.58 – 1.47 (m, 3H), 1.35 – 1.25 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 182.7, 160.1, 154.3, 139.1, 129.6, 126.0, 121.4, 121.0, 92.0, 67.9, 39.0, 29.5, 28.7, 21.1; **HRMS** calcd. for $C_{14}H_{14}Cl_3N_2O^+$ $[M + H]^+$ 331.0166, found 331.0167.

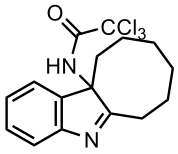
2,2,2-Trichloro-*N*-(7,8,9,10-tetrahydrocyclohepta[b]indol-10a(6H)-yl)acetamide (3t)



Following the **general procedure I**, *N*-hydroxyindole **1t** (105 mg, 0.523 mmol) afforded indolenine **3t** (136 mg, 75%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

***R*$_f$**=0.25 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.11 (s, 1H), 3.09 – 3.01 (m, 1H), 2.85 (dt, *J* = 17.2, 5.2 Hz, 1H), 2.37 (dt, *J* = 14.9, 3.8 Hz, 1H), 1.97 – 1.40 (m, 7H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 184.6, 159.7, 153.4, 139.9, 129.5, 126.2, 120.6, 120.5, 92.1, 71.8, 37.2, 32.5, 28.4, 26.0, 24.8; **HRMS** calcd. for $C_{15}H_{16}Cl_3N_2O^+$ $[M + H]^+$ 345.0323, found 345.0324.

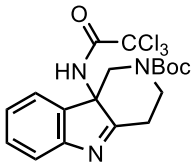
2,2,2-Trichloro-*N*-(6,7,8,9,10,11-hexahydro-11aH-cycloocta[b]indol-11a-yl)acetamide (3u)



Following the **general procedure I**, *N*-hydroxyindole **1u** (99.4 mg, 0.462 mmol) afforded indolenine **3u** (108 mg, 65%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

***R*$_f$**=0.38 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.26 – 7.19 (m, 2H), 6.94 (s, 1H), 2.87 – 2.80 (m, 2H), 2.65 (ddd, *J* = 13.9, 8.3, 5.5 Hz, 1H), 2.43 – 2.37 (m, 1H), 2.19 – 2.14 (m, 1H), 2.08 – 1.92 (m, 2H), 1.63 – 1.42 (m, 5H), 1.02 – 0.93 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 184.8, 159.6, 154.2, 138.1, 129.7, 126.3, 121.1, 120.6, 92.0, 70.9, 34.3, 29.7, 27.4, 27.2, 24.7, 20.9; **HRMS** calcd. for $C_{16}H_{18}Cl_3N_2O^+$ $[M + H]^+$ 359.0479, found 359.0477.

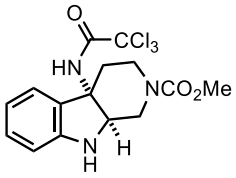
***tert*-Butyl 9b-(2,2,2-trichloroacetamido)-1,3,4,9b-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate (3v)**



Following the **general procedure I**, *N*-hydroxyindole **1v** (55.3 mg, 0.203 mmol) afforded indolenine **3v** (46.6 mg, 53%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

***R*$_f$**=0.36 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.38 (br s, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 1H), 5.00 (dd, *J* = 14.2, 2.5 Hz, 1H), 4.51 (dd, *J* = 12.5, 5.4 Hz, 1H), 2.94 (dd, *J* = 13.3, 2.3 Hz, 2H), 2.87 (td, *J* = 12.7, 3.2 Hz, 1H), 2.69 (td, *J* = 12.4, 6.3 Hz, 1H), 2.22 (d, *J* = 14.2 Hz, 1H), 1.54 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 179.0, 160.8, 157.0, 154.7, 135.1, 130.2, 126.4, 121.7, 121.5, 91.5, 82.3, 70.6, 53.9, 46.9, 30.9, 28.6; **HRMS** calcd. for $C_{18}H_{21}Cl_3N_3O_3^+$ $[M + H]^+$ 432.0643, found 432.0641.

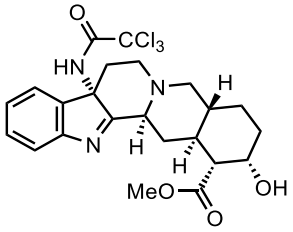
Methyl 4a-(2,2,2-trichloroacetamido)-1,3,4,4a,9,9a-hexahydro-2H-pyrido[3,4-b]indole-2-carboxylate (3w)



Following the **general procedure I**, *N*-hydroxyindole **1w** (50.6 mg, 0.205 mmol) afforded corresponding pyrroloindoline, which was then subsequently reduced due to its lability to afford indoline **3w** (32.2 mg, 40% for 2 steps) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

***R*$_f$**=0.25 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 4.84 (s, 1H), 3.88 (d, *J* = 10.4 Hz, 1H), 3.80 (d, *J* = 10.4 Hz, 1H), 3.64 (s, 3H), 3.35 – 3.11 (m, 2H), 2.55 – 2.49 (m, 1H), 2.30 – 2.23 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 161.1, 157.2, 150.7, 130.3, 129.0, 123.1, 119.6, 110.9, 92.7, 65.0, 58.1, 52.3, 37.1, 36.7, 31.1; **HRMS** calcd. for $C_{15}H_{17}Cl_3N_3O_3^+$ $[M + H]^+$ 392.0330, found 392.0325.

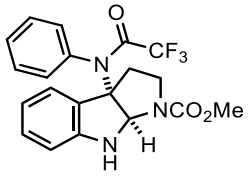
Methyl (1R,2S,4aR,8aS,13bS,14aS)-2-hydroxy-8a-(2,2,2-trichloroacetamido)-1,2,3,4,4a,5,7,8,8a,13b,14,14a-dodecahydroindolo[2',3':3,4]pyrido[1,2-b]isoquinoline-1-carboxylate (3x)



Following the **general procedure I**, *N*-hydroxyindole **1x** (40.0 mg, 0.108 mmol) afforded indolenine **3x** (24.5 mg, 44%) as a pale yellow oil after purification by flash column chromatography (silica gel, CH_2Cl_2:MeOH = 1:0 → 9:1).

***R**f*=0.30 (silica gel, CH_2Cl_2:MeOH = 9:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.6 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 6.89 (s, 1H), 4.19 (s, 1H), 3.77 (s, 3H), 3.15 (s, 1H), 2.94 (ddd, *J* = 20.8, 10.9, 3.0 Hz, 2H), 2.83 (d, *J* = 12.0 Hz, 1H), 2.68 (d, *J* = 14.5 Hz, 1H), 2.60 (t, *J* = 12.9 Hz, 1H), 2.38 (d, *J* = 11.1 Hz, 1H), 2.18 (t, *J* = 10.8 Hz, 1H), 2.12 – 2.07 (m, 1H), 1.96 (ddd, *J* = 13.6, 10.6, 2.7 Hz, 2H), 1.93 – 1.81 (m, 2H), 1.64 – 1.35 (m, 5H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 178.7, 176.0, 160.1, 154.3, 138.7, 129.9, 126.7, 121.9, 121.7, 92.1, 66.9, 66.8, 61.6, 60.3, 52.2, 52.1, 50.1, 40.5, 36.5, 36.4, 31.4, 31.2, 23.2; **HRMS** calcd. for $C_{23}H_{27}Cl_3N_3O_4^+$ $[M + H]^+$ 514.1062, found 514.1053.

Methyl 3a-(2,2,2-trifluoro-*N*-phenylacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3y)

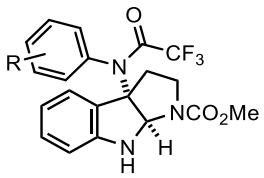


Following the **general procedure K**, *N*-hydroxyindole **1a** (188 mg, 0.803 mmol) and imidoyl chloride **R1** (248 mg, 1.20 mmol) afforded pyrroloindoline **3y** (97.7 mg, 30%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

***R**f*=0.42 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 8.02 and

7.94 (s, 1H), 7.50 (d, J = 8.3 Hz, 2H), 7.40 – 7.36 (m, 2H), 7.10 (t, J = 7.6 Hz, 1H), 7.03 (t, J = 6.6 Hz, 1H), 6.81 – 6.73 (m, 1H), 6.68 (d, J = 7.7 Hz, 1H), 5.46 and 5.41 (s, 1H), 5.22 and 4.79 (s, 1H), 3.92 and 3.80 (t, J = 9.1 Hz, 1H), 3.79 and 3.71 (s, 3H), 3.15 (q, J = 9.1, 8.6 Hz, 1H), 2.66 – 2.56 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 155.5, 154.9 (q, J = 36.9 Hz),154.6, 149.0, 148.8, 142.1, 142.0, 134.1, 134.0, 131.9, 131.8, 129.0, 128.9, 126.9, 126.8, 124.0, 123.9, 120.9, 119.9, 119.6, 115.8 (d, J = 288.7 Hz), 110.3, 110.1, 82.9, 82.5, 61.2, 60.0, 52.9, 52.6, 46.5, 46.2, 36.1, 35.9; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −75.7, −75.6; **HRMS** calcd. for $C_{20}H_{19}F_3N_3O_3^+$ $[M + H]^+$ 406.1373, found 406.1372.

Methyl 3a-(*N*-(2,6-dimethylphenyl)-2,2,2-trifluoroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3z)

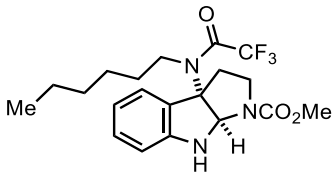


R= 2,6-Me_2

Following the **general procedure K**, *N*-hydroxyindole **1a** (150 mg, 0.642 mmol) and imidoyl chloride **R2** (227 mg, 0.963 mmol) afforded pyrroloindoline **3z** (47.3 mg, 17%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

***R*$_f$**=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.42 (s, 1H), 7.12 – 7.08 (m, 3H), 7.05 ad 7.03 (d, J = 7.4 Hz, 1H), 6.77 (td, J = 7.4, 3.0 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 5.48 and 5.42 (s, 1H), 5.20 and 4.76 (s, 1H), 3.91 and 3.79 (t, J = 8.6 Hz, 1H), 3.79 and 3.71 (s, 3H), 3.17 – 3.09 (m, 1H), 2.63 – 2.54 (m, 2H), 2.19 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 155.7 (q, J = 36.4 Hz), 155.5, 154.6, 149.1, 148.8, 144.3, 144.2, 135.6, 131.9, 131.8, 129.6, 128.9, 128.9, 126.1, 124.1, 124.0, 119.8, 119.5, 116.2 (q, J = 288.8 Hz), 110.3, 110.1, 83.0, 82.5, 61.2, 60.0, 52.9, 52.5, 46.5, 46.2, 36.5, 36.2, 18.4; **^{19}F NMR** (471 MHz, $CDCl_3$): δ −75.3; **HRMS** calcd. for $C_{22}H_{23}F_3N_3O_3^+$ $[M + H]^+$ 434.1686, found 434.1683.

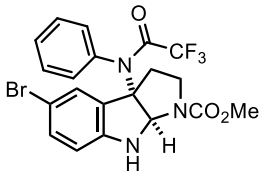
Methyl 3a-(2,2,2-trifluoro-*N*-hexylacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3aa)



Following the **general procedure K**, *N*-hydroxyindole **1a** (129 mg, 0.551 mmol) and imidoyl chloride **R3** (178 mg, 0.825 mmol) afforded pyrroloindoline **3aa** (34.5 mg, 15%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

***R**f*=0.65 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.34 and 7.30 (d, *J* = 7.4 Hz, 1H), 7.23 – 7.19 (m, 1H), 6.83 (q, *J* = 8.2 Hz, 1H), 6.66 (d, *J* = 7.9 Hz, 1H), 5.71 and 5.70 (s, 1H), 3.92 – 3.86 and 3.80 – 3.76 (m, 1H), 3.76 and 3.68 (s, 3H), 3.29 (dq, *J* = 11.2, 6.5, 4.8 Hz, 2H), 3.11 – 2.93 (m, 2H), 2.45 – 2.42 and 2.33 – 2.28 (m, 1H), 1.39 – 1.24 (m, 2H), 1.14 – 1.07 (m, 3H), 1.04 – 0.96 (m, 3H), 0.86 (t, *J* = 6.8 Hz, 1H), 0.78 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 157.6 (q, *J* = 35.6 Hz), 155.6, 154.7, 151.0, 150.9, 131.2, 131.1, 126.7, 126.6, 125.6, 125.1, 119.6, 119.3, 116.5 (q, *J* = 288.4 Hz), 110.6, 110.6, 78.3, 52.9, 52.6, 46.6, 46.5, 46.1, 45.8, 33.5, 32.6, 31.0, 30.4, 26.1, 26.0, 22.4, 14.0; **^{19}F NMR** (471 MHz, $CDCl_3$): δ –69.4; **HRMS** calcd. for $C_{20}H_{27}F_3N_3O_3^+$ $[M + H]^+$ 414.1999, found 414.1991.

Methyl 5-bromo-3a-(2,2,2-trifluoro-*N*-phenylacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3ab)

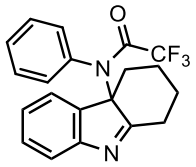


Following the **general procedure K**, *N*-hydroxyindole **1g** (0.150 g, 0.479 mmol) and imidoyl chloride **R1** (149 mg, 0.718 mmol) afforded pyrroloindoline **3ab** (48.7 mg, 21%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

***R**f*=0.42 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.89 (br s, 1H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.39 – 7.35 (m, 2H), 7.21 – 7.17 (m, 1H), 7.10 – 7.07 (m, 1H), 6.56 (d, *J* = 8.3 Hz,

1H), 5.47 and 5.42 (s, 1H), 3.94 and 3.81 (t, J = 9.3 Hz, 1H), 3.78 and 3.72 (s, 3H), 3.17 (td, J = 10.8, 5.9 Hz, 1H), 2.67 – 2.54 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 155.5, 154.9 (q, J = 38.7 Hz), 154.5, 148.1, 147.8, 141.4, 141.3, 134.5, 1345, 134.3, 134.3, 131.8, 131.7, 127.0, 126.9, 126.7, 126.7, 120.9, 115.8 (q, J = 288.8 Hz), 111.7, 111.5, 111.3, 111.0, 83.1, 82.7, 61.2, 60.0, 53.0, 52.7, 46.4, 46.1, 35.9, 35.7; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −75.7; **HRMS** calcd. for $C_{20}H_{18}BrF_3N_3O_3^+$ $[M + H]^+$ 484.0478, found 484.0475.

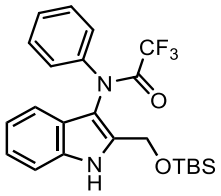
2,2,2-Trifluoro-*N*-phenyl-*N*-(1,2,3,4-tetrahydro-4aH-carbazol-4a-yl)acetamide (3ac)



Following the **general procedure K**, *N*-hydroxyindole **1s** (72.0 mg, 0.385 mmol) and imidoyl chloride **R1** (0.120 g, 0.578 mmol) afforded pyrroloindoline **3ac** (43.2 mg, 31%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

***R*$_f$**=0.29 (silica gel, hexanes:EtOAc = 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84 (br s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.52 (d, J = 8.3 Hz, 2H), 7.30 (td, J = 7.5, 1.4 Hz, 2H), 7.16 – 7.02 (m, 4H), 3.11 (d, J = 14.1 Hz, 1H), 2.96 (d, J = 13.1 Hz, 1H), 2.50 (td, J = 12.8, 5.9 Hz, 1H), 2.16 – 2.12 (m, 1H), 1.79 – 1.51 (m, 3H), 1.39 – 1.27 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 188.6, 154.1, 147.2, 136.9, 134.1, 127.9, 127.4, 125.6, 122.4, 121.4, 120.8, 118.5 (q, J = 251.0 Hz), 62.6, 36.6, 30.7, 29.4, 22.0; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −75.7; **HRMS** calcd. for $C_{20}H_{18}F_3N_2O^+$ $[M + H]^+$ 359.1366, found 359.1366.

***N*-(2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-1H-indol-3-yl)-2,2,2-trifluoro-*N*-phenylacetamide (3ad)**

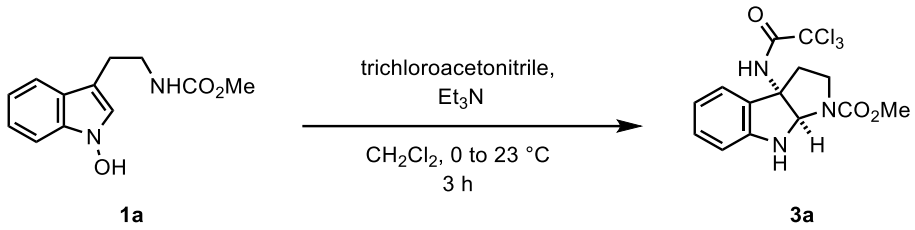


Following the **general procedure K**, *N*-hydroxyindole **1q** (55.0 mg, 0.198 mmol) and imidoyl chloride **R1** (61.7 mg, 0.297 mmol) afforded pyrroloindoline **3ad** (45.3 mg, 51%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5).

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, MeOD): δ 7.90 – 7.86 (m, 1H), 7.49 – 7.43 (m, 3H), 7.38 (td, *J* = 7.4, 1.4 Hz, 1H), 7.19 – 7.14 (m, 2H), 7.01 (td, *J* = 7.5, 7.0, 1.1 Hz, 1H), 4.78 (d, *J* = 12.5 Hz, 1H), 4.71 (d, *J* = 12.5 Hz, 1H), 0.86 (s, 9H), 0.00 and −0.01 (s, 6H); **^{13}C NMR** (126 MHz, MeOD): δ 154.7 (q, *J* = 37.3 Hz), 154.5, 136.3, 135.5, 134.1, 133.7, 131.8, 129.3, 128.6, 127.0, 126.0, 125.0, 123.1, 121.0, 119.0, 117.7, 115.7 (q, *J* = 288.8 Hz), 111.6, 107.0, 57.7, 26.0, 18.5, −5.4; **^{19}F NMR** (376 MHz, MeOD): δ −77.5; **HRMS** calcd. for $C_{23}H_{26}F_3N_2O_2Si^-$ $[M - H]^-$ 447.1721, found 447.1719.

5.4. Evaluation of Practicality and Versatility of the C3-Amidaiton (Scheme 4)

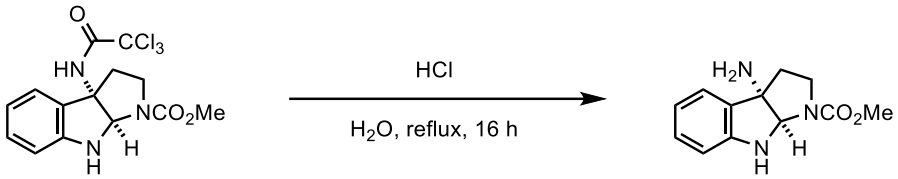
5.4.1. Gram-scale Reaction



1a **3a**

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1a** (1.01 g, 4.31 mmol, 1.0 equiv) and CH_2Cl_2 (50 mL) at 23 °C. The resulting solution was cooled to 0 °C, and trichloroacetonitrile (1.30 mL, 12.9 mmol, 3.0 equiv) and Et_3N (60 μL, 0.1 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 3 h before it was quenched with H_2O (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford pyrroloindoline **3a** (1.11 g, 68%) as a pale yellow oil.

5.4.2. Conversion to the 3-Aminopyrroloindoline

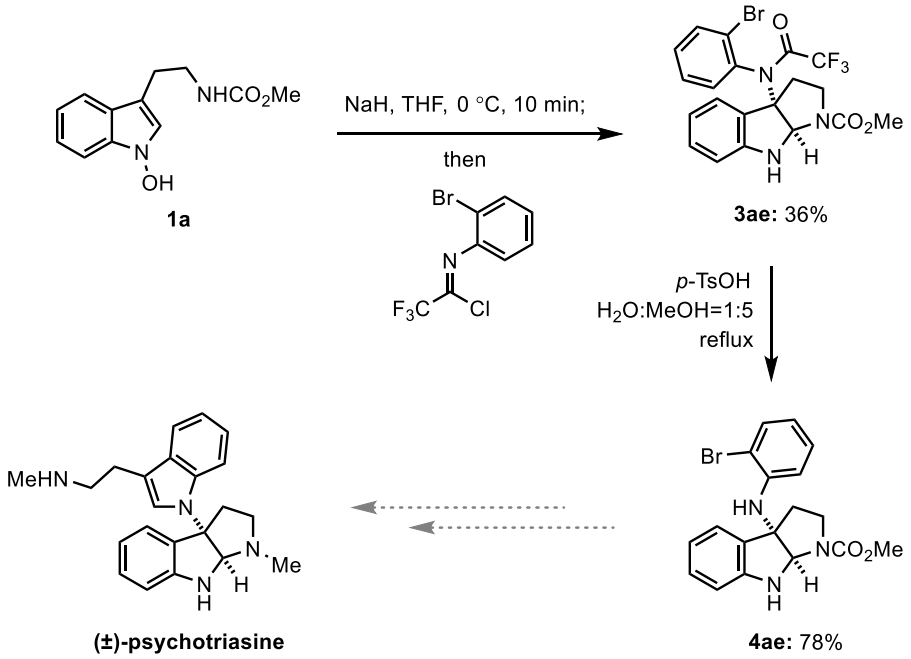


3a **4a**

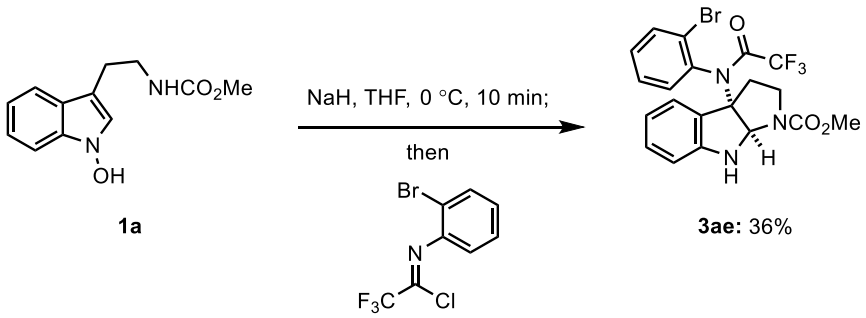
To an oven-dried round-bottom flask equipped with a stir bar and septum were added **3a** (0.100 g, 0.264 mmol, 1.0 equiv) and H_2O (5 mL) at 23 °C, followed by HCl (35.0–37.0 wt% in H_2O, 70 μL, 0.792 mmol, 3.0 equiv). The resulting mixture was heated to 100 °C in a pre-heated oil bath and stirred for 16 h. After the reaction mixture was cooled to 23 °C, the reaction mixture was quenched with EtOAc (5 mL) and quenched with $NaHCO_3$ (5 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, CH_2Cl_2:MeOH = 1:0 → 95:5) to afford pyrroloindoline **4a** (43.0 mg, 70%) as a pale yellow oil. Analytic data is in agreement with the reported literature values.[3]

***R**f*=0.35 (silica gel, CH_2Cl_2:MeOH = 9:1); **^{1}H NMR** (500 MHz, $CDCl_3$, 60:40 mixture of rotamers): δ 7.24 (d, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.82 – 6.78 (m, 1H), 6.62 (dd, *J* = 8.0, 3.2 Hz, 1H), 5.12 and 4.71 (s, 1H), 5.09 and 5.05 (s, 1H), 3.77 and 3.69 (s, 3H), 3.67 – 3.62 (m, 1H), 3.17 – 3.09 (m, 1H), 2.40 – 2.33 (m, 1H), 2.25 – 2.16 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 155.8, 155.0, 149.1, 148.8, 131.8, 129.7, 123.3, 119.7, 119.5, 110.1, 110.0, 83.6, 83.3, 70.7, 69.6, 52.8, 52.5, 46.1, 45.7, 37.8, 37.7; **HRMS** calcd. for $C_{12}H_{16}N_3O_2^+$ $[M + H]^+$ 234.1237, found 234.1238.

5.4.3. Formal Synthesis of Psychotriasine



Methyl 3a-(*N*-(2-bromophenyl)-2,2,2-trifluoroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3ae)

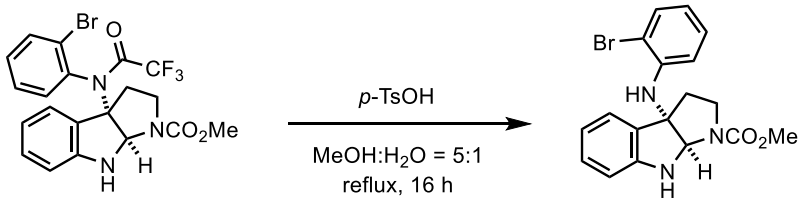


To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole **1a** (0.100 g, 0.427 mmol, 1.0 equiv) and THF (8 mL) at 23 °C. The resulting solution was cooled to 0 °C, and NaH (60% in mineral oil, 25.6 mg, 0.641 mmol, 1.5 equiv) was added to the solution. The reaction mixture was stirred for 10 min, then *N*-(2-bromophenyl)-2,2,2-trifluoroacetimidoyl chloride (0.184 g, 0.641 mmol, 1.5 equiv) was added. The resulting mixture was stirred for additional 1 h at 0 °C before it was quenched with H_2O (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure.

The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford pyrroloindoline **3ae** (74.0 mg, 36%) as a yellow oil.

***R**f*=0.47 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 8.22 (d, *J* = 8.6 Hz, 1H), 7.59 (dd, *J* = 7.8, 2.1 Hz, 1H), 7.41 – 7.38 (m, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.1 Hz, 1H), 6.80 – 6.76 (m, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 5.45 and 5.40 (s, 1H), 5.24 and 4.80 (s, 1H), 3.96 – 3.91 and 3.83 – 3.79 (m, 1H), 3.79 and 3.71 (s, 3H), 3.18 – 3.10 (m, 1H), 2.62 – 2.57 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ 155.5, 154.76 (d, *J* = 37.1 Hz). 154.5, 149.0, 148.7, 143.4, 143.3, 132.1, 131.2, 130.0, 129.2, 126.2, 123.9, 123.8, 122.2, 122.1, 120.0, 119.7, 115.67 (q, *J* = 288.7 Hz), 114.5, 110.5, 110.3, 82.8, 82.3, 60.9, 59.7, 52.9, 52.6, 46.4, 46.1, 36.0, 35.7; **^{19}F NMR** (471 MHz, $CDCl_3$): δ −75.8; **HRMS** calcd. for $C_{20}H_{18}BrF_3N_3O_3^+$ $[M + H]^+$ 484.0478, found 484.0479.

Methyl 3a-((2-bromophenyl)amino)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (4ae)



3ae **4ae**

To an oven-dried round-bottom flask equipped with a stir bar and septum were added **3ae** (56.0 mg, 0.116 mmol, 1.0 equiv) and MeOH:H_2O (5:1, 3 mL) at 23 °C, followed by *p*-TsOH (59.9 mg, 0.348 mmol, 3.0 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h. After the reaction mixture was cooled to 23 °C, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and quenched with $NaHCO_3$ (10 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford pyrroloindoline **4ae** (35.0 mg, 78%) as a yellow oil. Analytic data is in agreement with the reported literature values.[3]

***R**f*=0.24 (silica gel, hexanes:EtOAc = 7:3); **^{1}H NMR** (500 MHz, $CDCl_3$, 50:50 mixture of rotamers): δ 7.41 (t, *J* = 8.1 Hz, 1H), 7.16 (t, *J* = 9.1 Hz, 2H), 6.98 (t, *J* = 7.9 Hz, 1H), 6.77 (q, *J* = 7.2 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.57 – 6.54 (m, 1H), 6.44 (dd, *J* = 16.5, 8.2 Hz, 1H), 5.73 and 5.66 (s, 1H), 5.14 and 4.82 (s, 1H), 4.81 and 4.77

(s, 1H), 3.90 – 3.85 and 3.79 – 3.75 (m, 1H), 3.77 and 3.74 (s, 3H), 3.35 – 3.28 (m, 1H), 2.65 – 2.55 (m, 1H), 2.42 – 2.36 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 156.1, 155.2, 149.1, 148.9, 142.2, 132.8, 132.7, 130.0, 129.1, 129.0, 128.4, 123.5, 123.4, 119.8, 119.6, 119.1, 119.0, 114.3, 114.0, 111.4, 111.3, 109.8, 109.7, 78.3, 73.5, 72.3, 52.9, 52.7, 44.7, 44.5, 39.2, 38.9; **HRMS** calcd. for $C_{18}H_{19}BrN_3O_2^+$ $[M + H]^+$ 388.0655, found 388.0659.

6. Abbreviations

BHT	2,6-di-*tert*-butyl-4-methylphenol
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene
DCC	*N,N'*-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DIPEA	*N,N*-diisopropylethylamine
DMAP	4-(dimethylamino)pyridine
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
EtOAc	ethyl acetate
EDC·HCl	1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydro-chloride
LC-MS	liquid chromatography–mass spectrometry
HOBt	hydroxybenzotriazole
HPLC	high-performance liquid chromatography
HRMS	high-resolution mass spectrometry
IHT	indolyl 1,3-heteroatom transposition
LAH	lithium aluminium hydride
LDA	lithium diisopropylamide
LiHMDS	lithium bis(trimethylsilyl)amide

Me	methyl
MeCN	acetonitrile
ppm	parts per million
TBSCl	*tert*-butyldimethylsilyl chloride
TCE	1,1,2,2-tetrachloroethane
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin-layers chromatography
p-TsOH	*para*-toluenesulfonic acid

7. References

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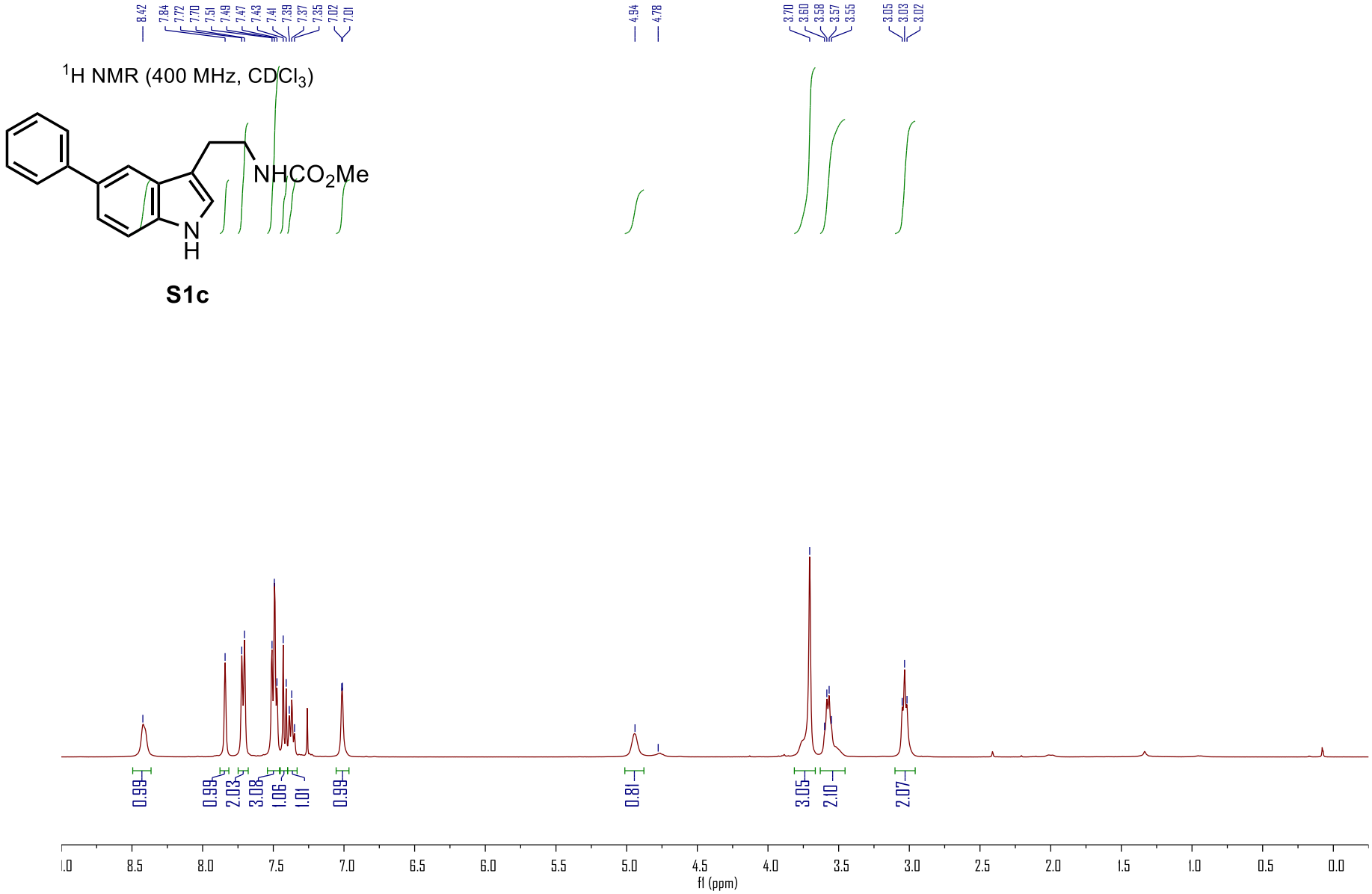
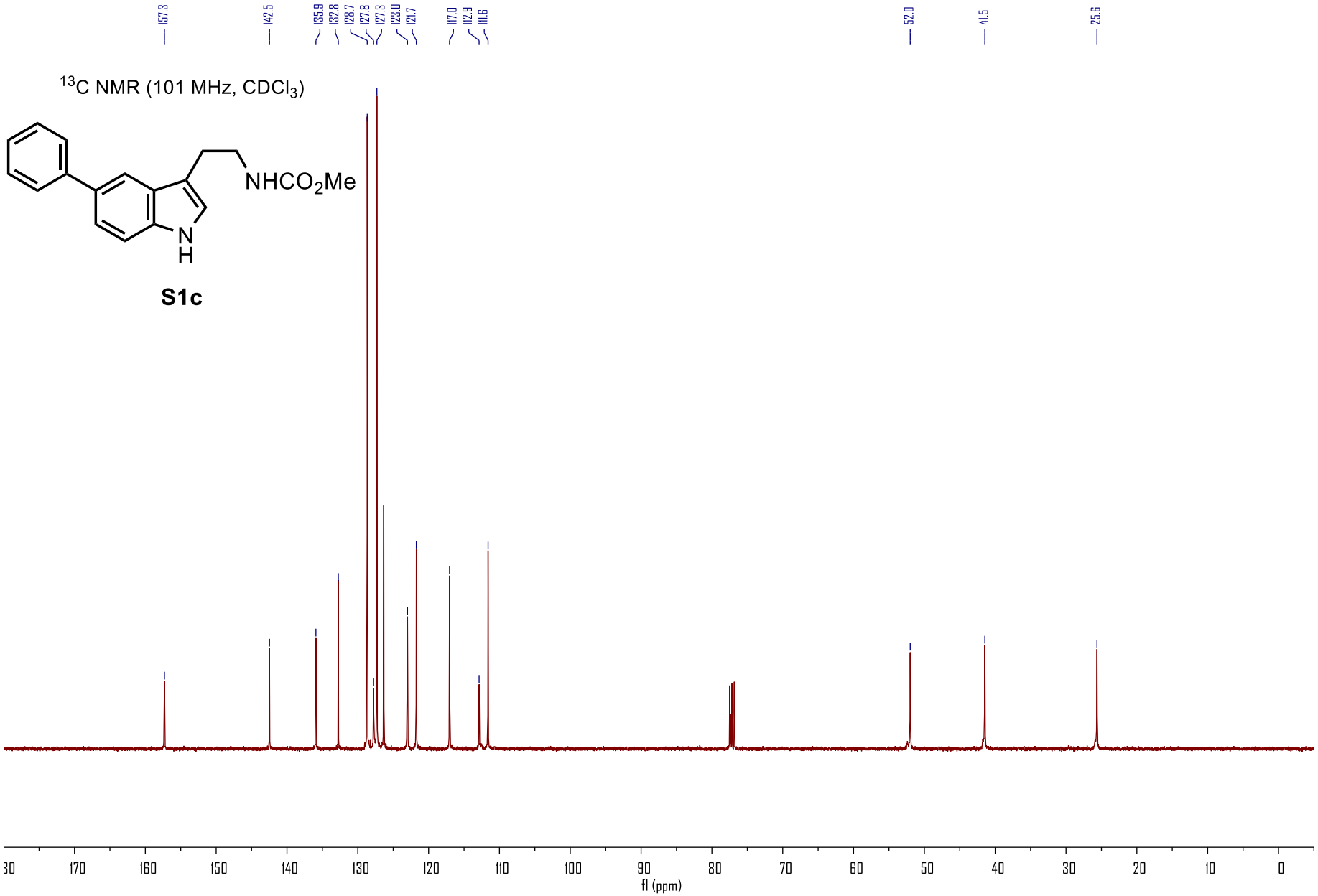
8. NMR Spectra

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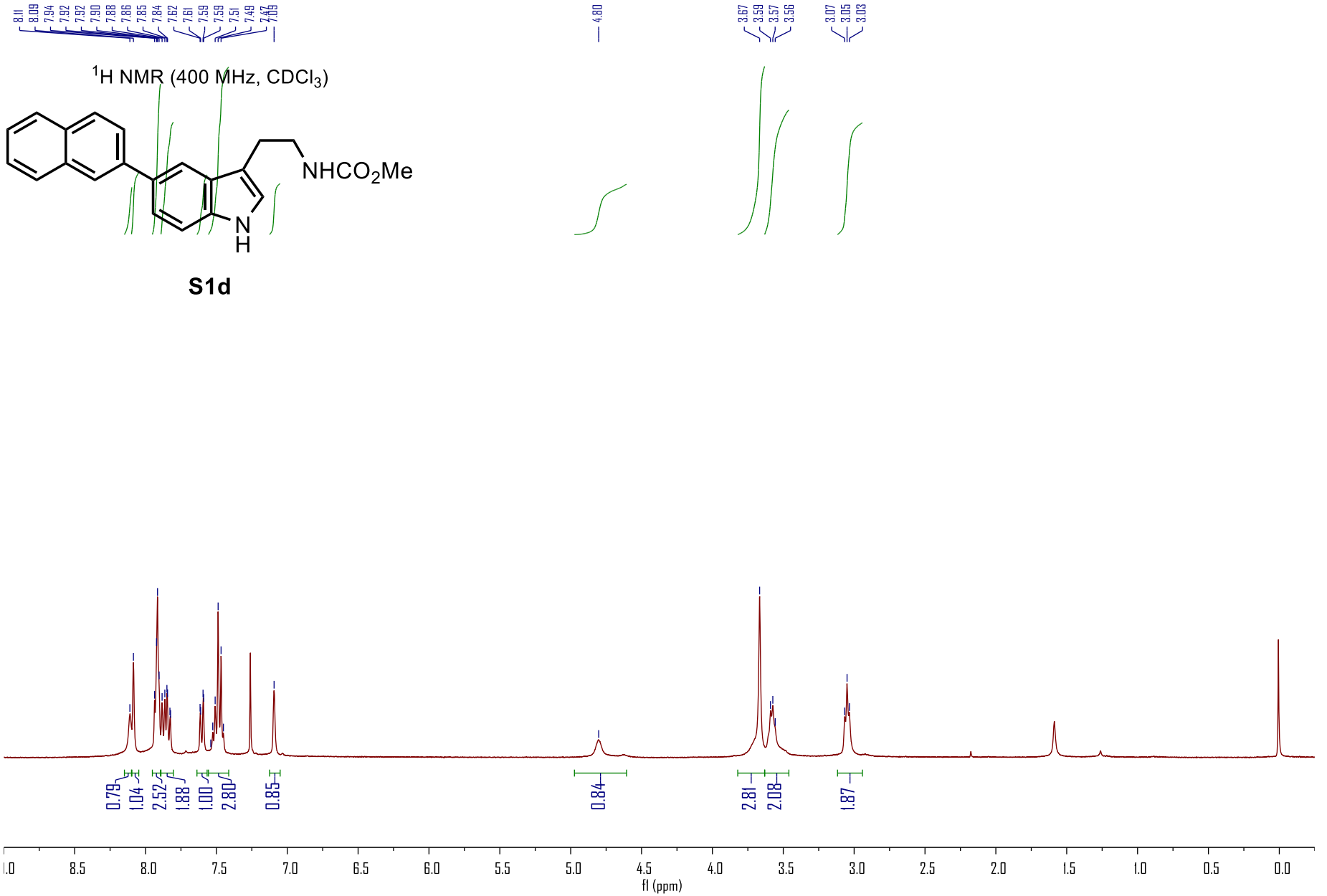
142.5
135.9
132.8
128.7
127.8
127.3
123.0
121.7
117.0
112.9
111.6
52.0
41.5
25.6
^{13}C NMR (101 MHz, $CDCl_3$)
NHCO$_2$Me
N
H
S1c
f1 (ppm)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7.94
7.92
7.92
7.90
7.88
7.86
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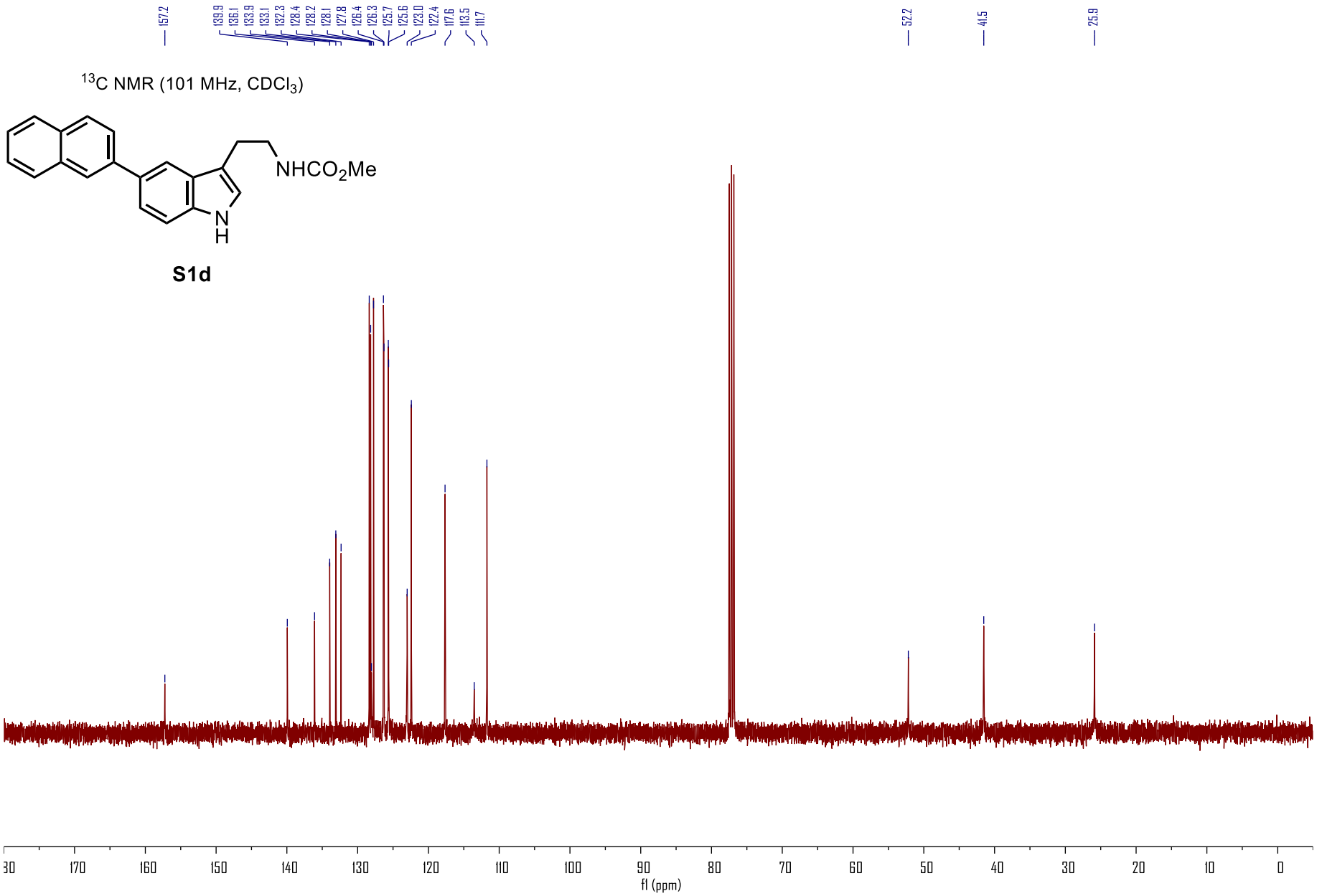
7.84
7.62
7.61
7.59
7.59
7.51
7.49
7.47
7.09
4.80
3.67
3.59
3.57
3.56
3.07
3.05
3.03
^{1}H NMR (400 MHz, $CDCl_3$)
$NHCO_2Me$
N
H
0.79
1.04
2.52
1.88
1.00
2.80
0.85
0.84
2.81
2.08
1.87
f1 (ppm)

S1d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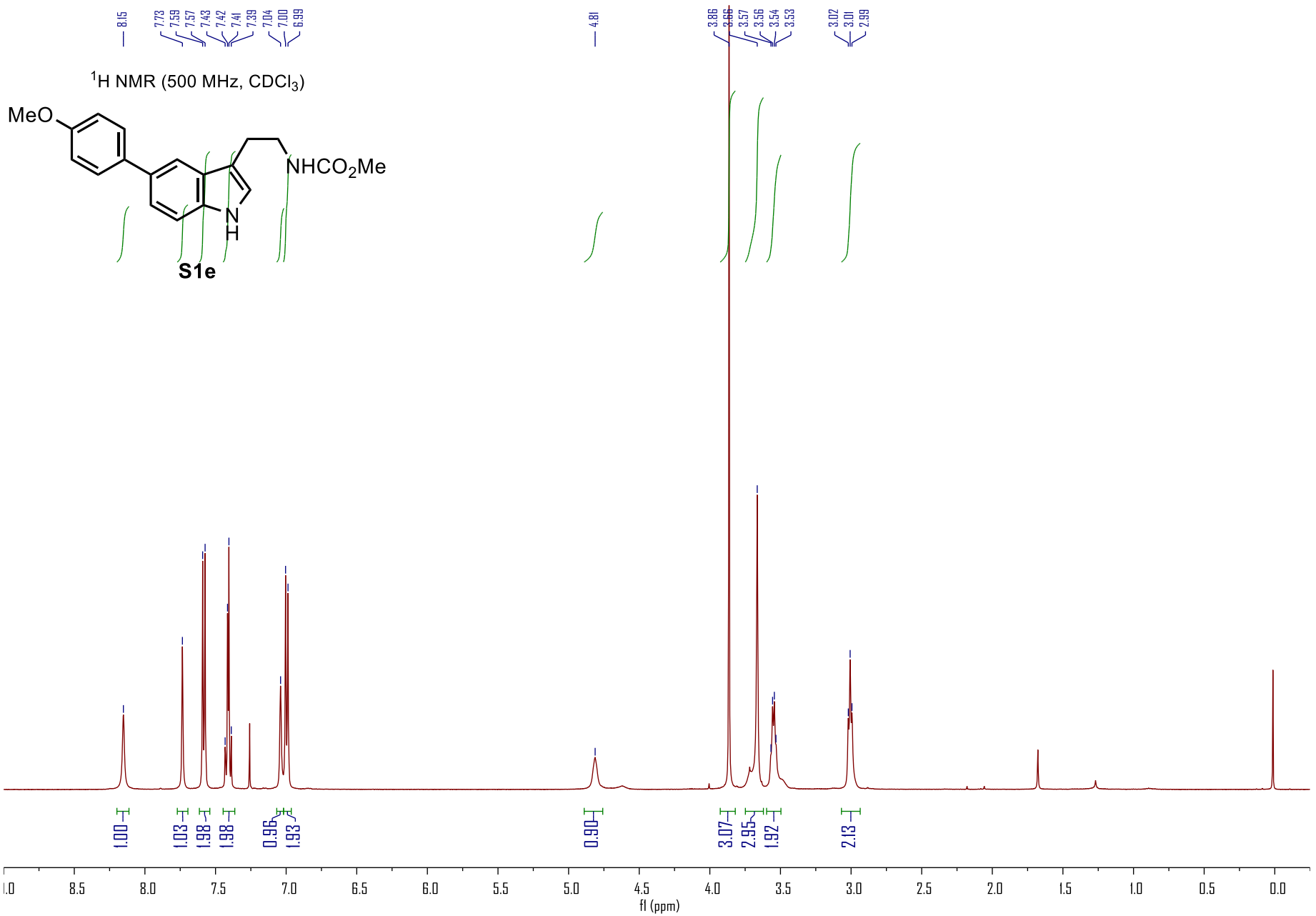
139.9
136.1
133.9
133.1
132.3
128.4
128.2
128.1
127.8
126.4
126.3
125.7
125.6
123.0
122.4
117.6
113.5
111.7
52.2
41.5
25.9
^{13}C NMR (101 MHz, $CDCl_3$)
NHCO$_2$Me
N
H
S1d
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.59
7.57
7.43
7.42
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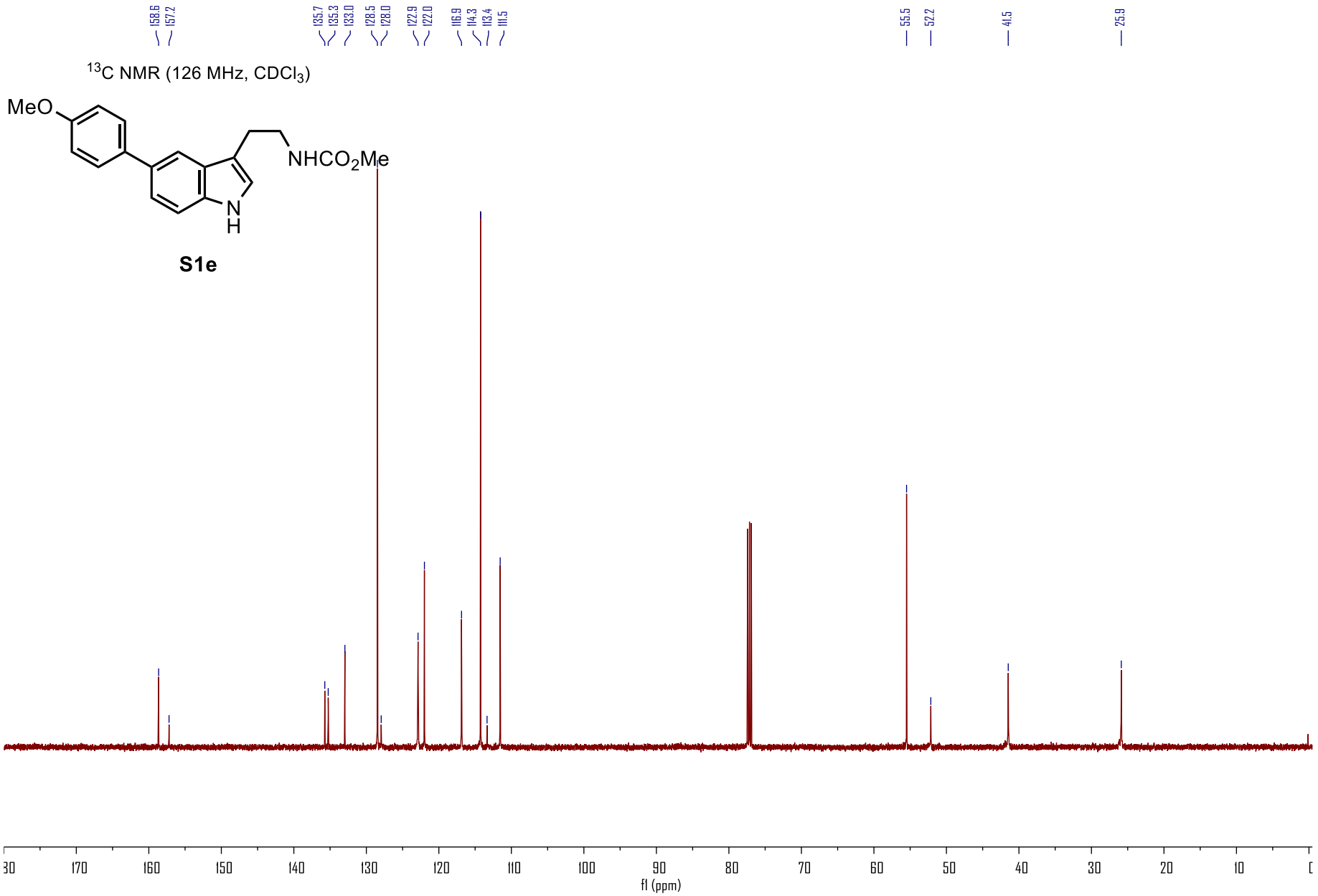
7.39
7.04
7.00
6.99
4.81
3.86
3.85
3.57
3.56
3.54
3.53
3.02
3.01
2.99
^{1}H NMR (500 MHz, $CDCl_3$)
MeO
NHCO$_2$Me
N
H
S1e
1.00
1.03
1.98
1.98
0.96
1.93
0.90
3.07
2.95
1.92
2.13
f1 (ppm)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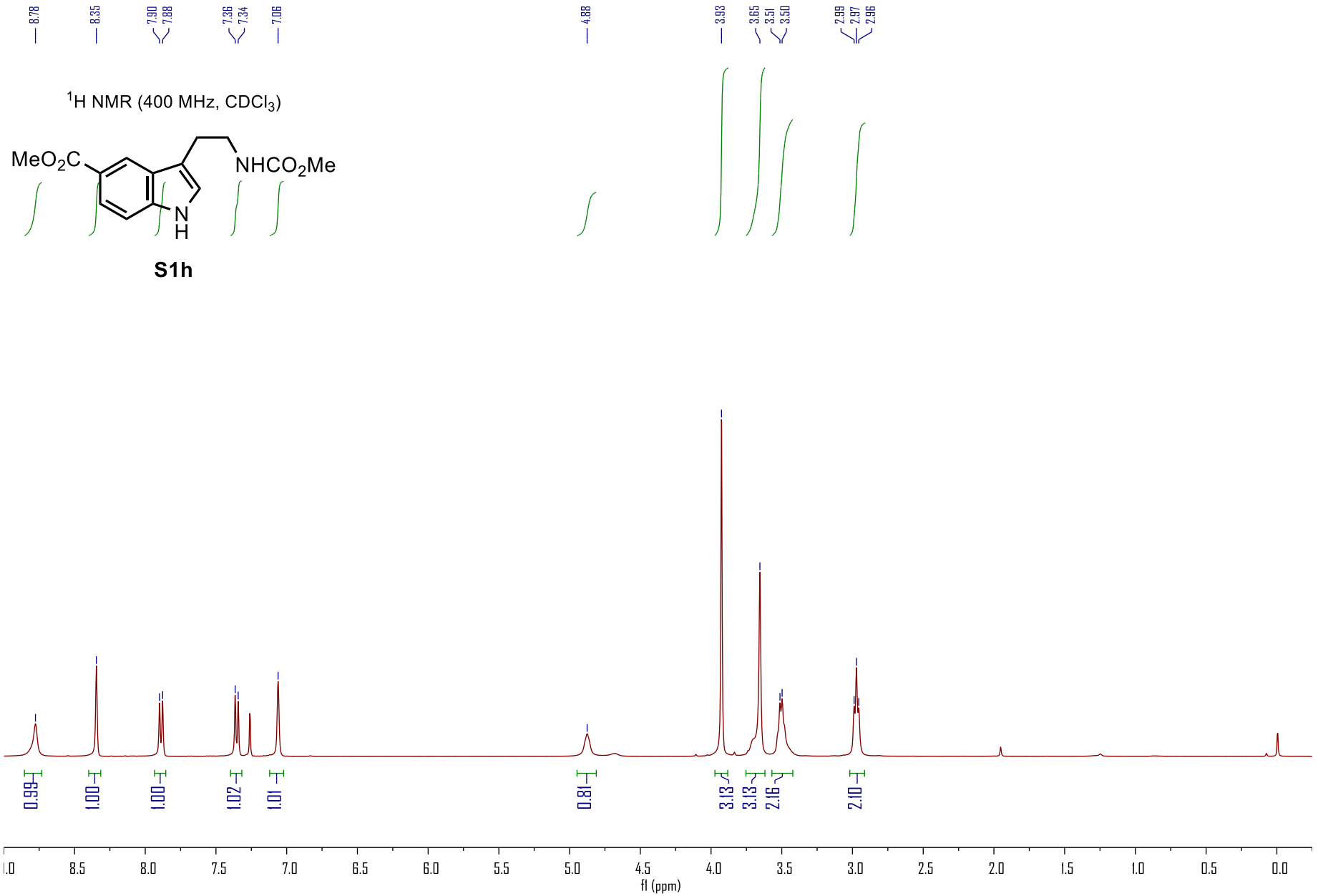
157.2
135.7
135.3
133.0
128.5
128.0
122.9
122.0
116.9
114.3
113.4
111.5
55.5
52.2
41.5
25.9
^{13}C NMR (126 MHz, $CDCl_3$)
MeO
NHCO$_2$Me
N
H
S1e
f1 (ppm)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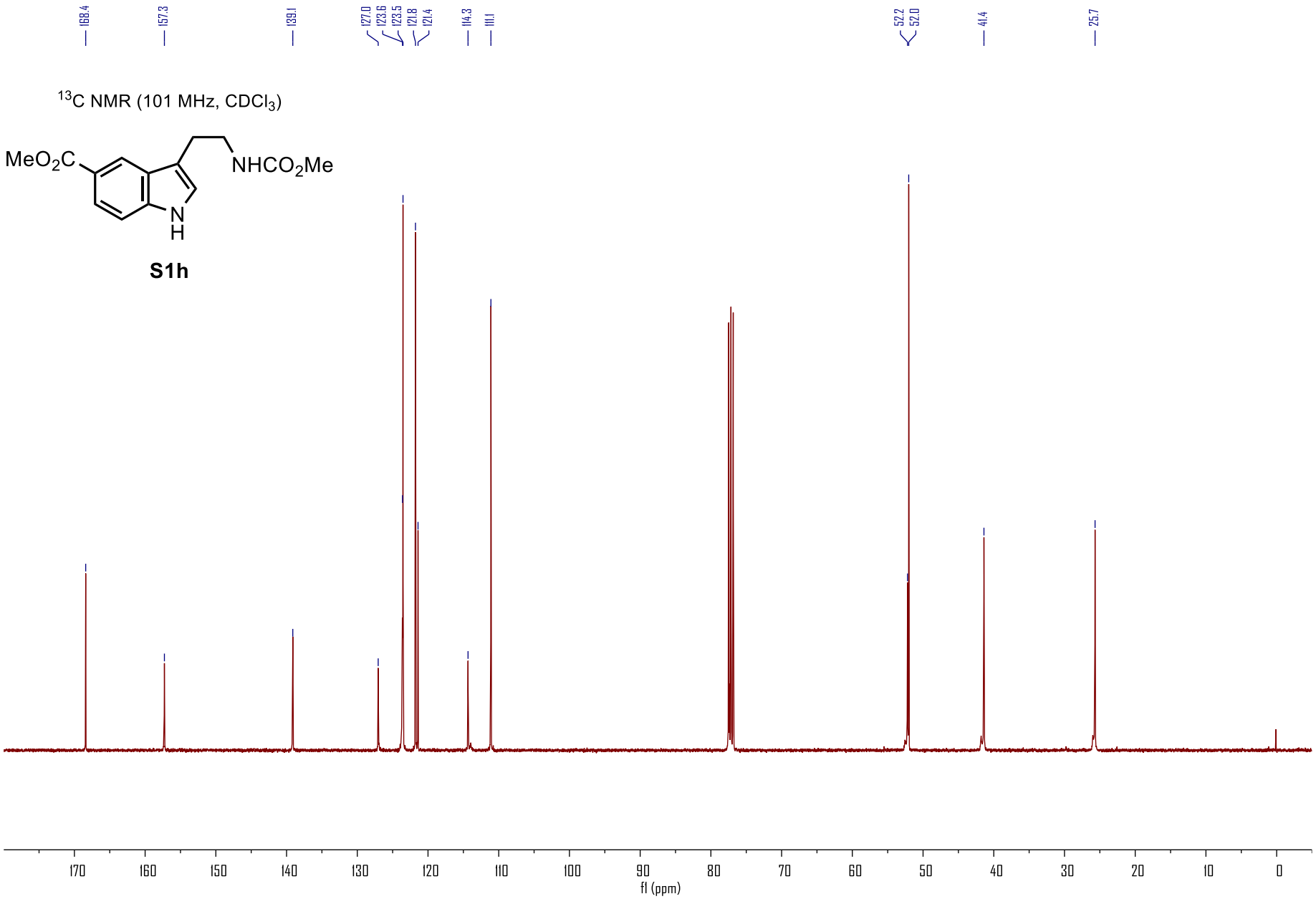
7.90
7.88
7.38
7.34
7.06
4.88
3.93
3.65
3.51
3.50
2.99
2.97
2.96
^{1}H NMR (400 MHz, $CDCl_3$)
MeO_2C
$NHCO_2Me$
N
H
0.99
1.00
1.00
1.02
1.01
0.81
3.13
3.13
2.16
2.10
f1 (ppm)

S1h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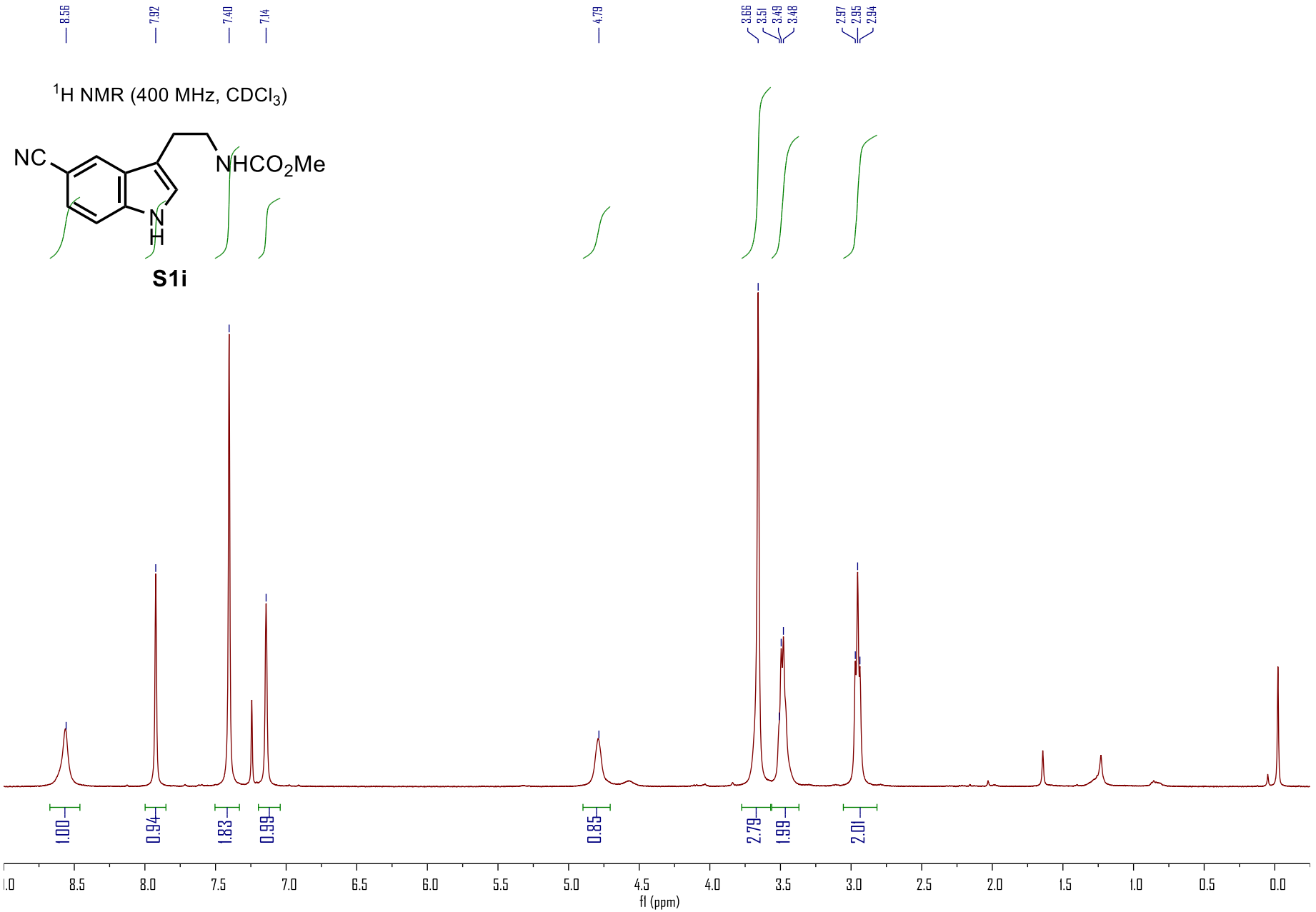
157.3
139.1
127.0
123.6
123.5
121.8
121.4
114.3
111.1
52.2
52.0
41.4
25.7
13C NMR (101 MHz, CDCl3)
MeO2C
NHCO2Me
N
H
S1h
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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4.79
3.66
3.51
3.49
3.48
2.97
2.95
2.94
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NC
$NHCO_2Me$
N
H
S1i
1.00
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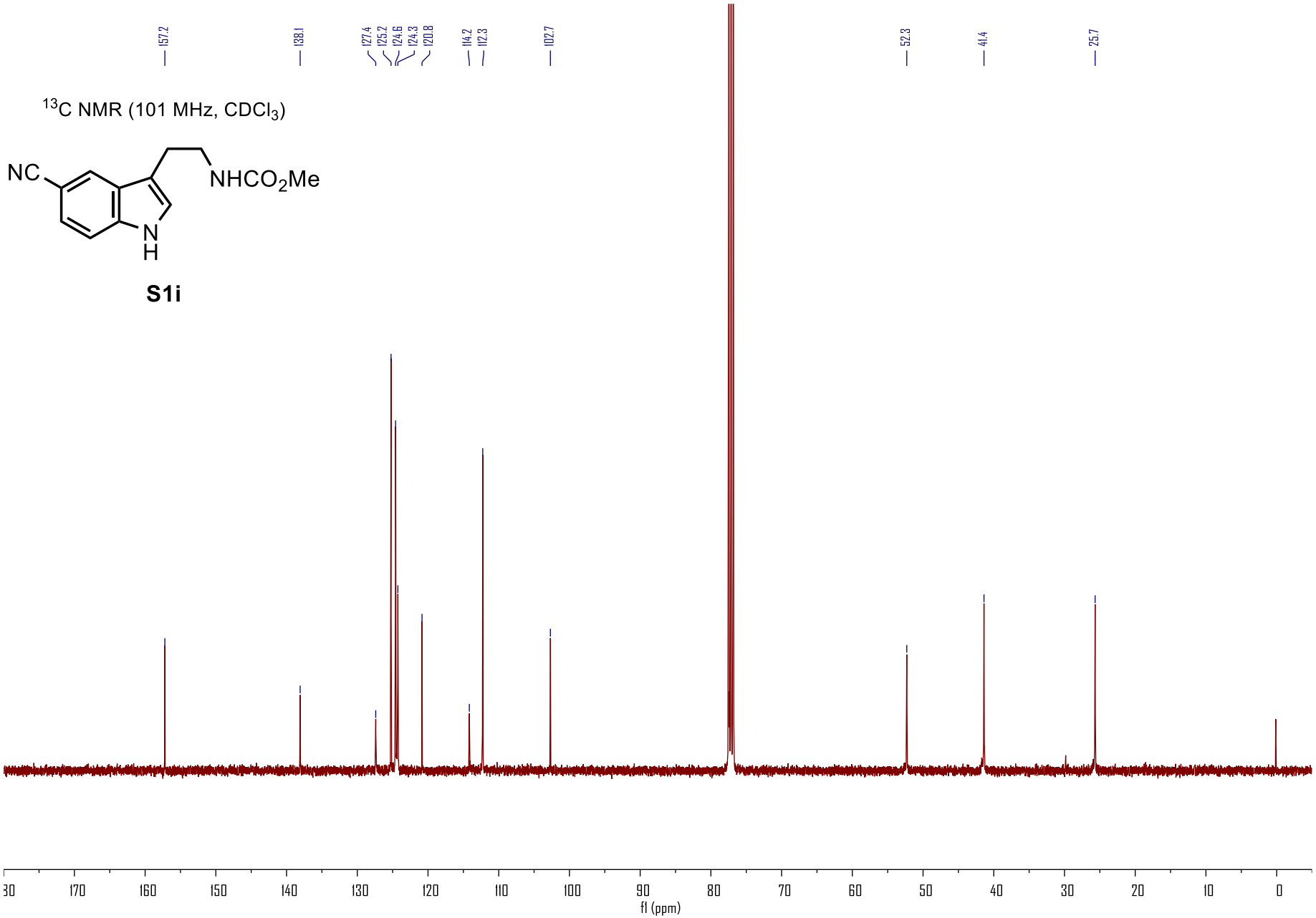
1.83
0.99
0.85
2.79
1.99
2.01
f1 (ppm)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127.4
125.2
124.6
124.3
120.8
114.2
112.3
102.7
52.3
41.4
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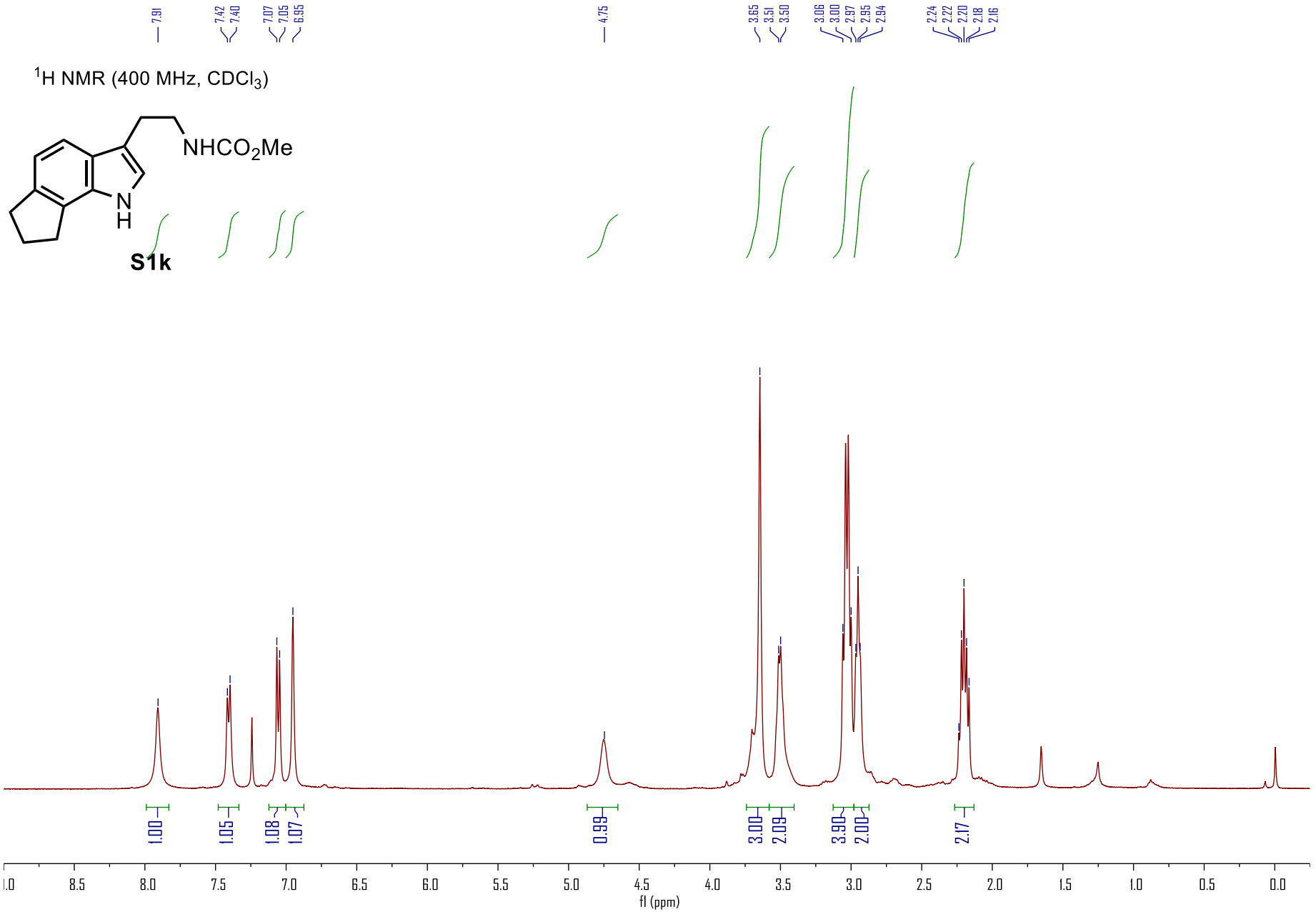
NC
$NHCO_2Me$
N
H
S1i
f1 (ppm)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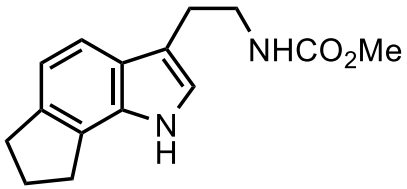
4.75
3.65
3.51
3.50
3.06
3.00
2.97
2.95
2.94
2.24
2.22
2.20
2.18
2.16
^{1}H NMR (400 MHz, $CDCl_3$)
NHCO$_2$Me
N
H
S1k
1.00
1.05
1.08
1.07
0.99
3.00
2.09
3.90
2.00
2.17
f1 (ppm)

^{13}C NMR (101 MHz, $CDCl_3$)



S1k

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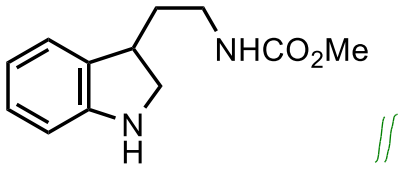
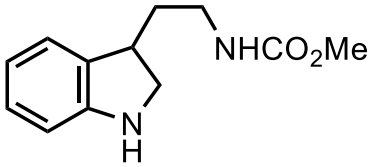


S2a

^{13}C NMR (126 MHz, $CDCl_3$)



S2a

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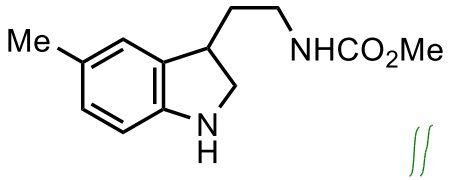
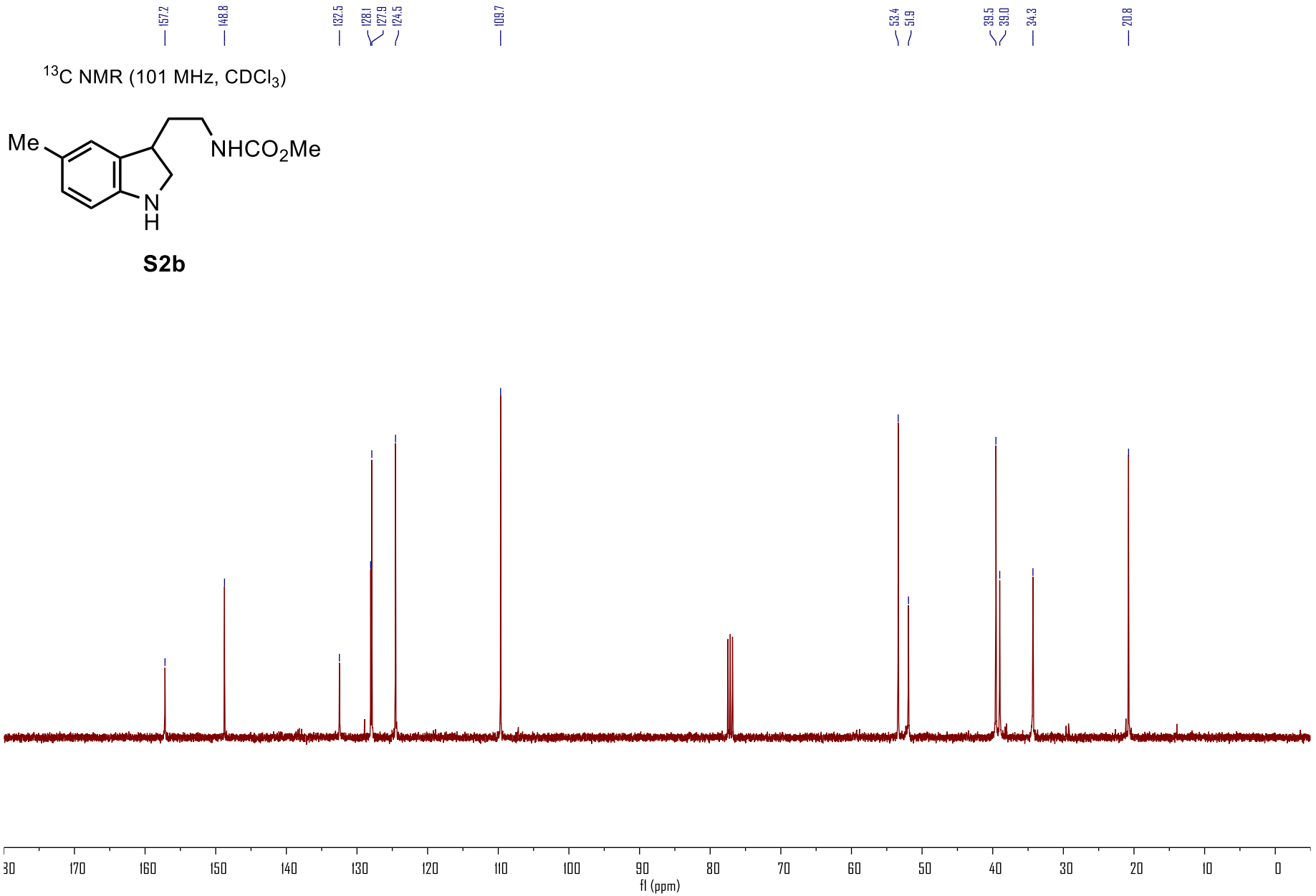
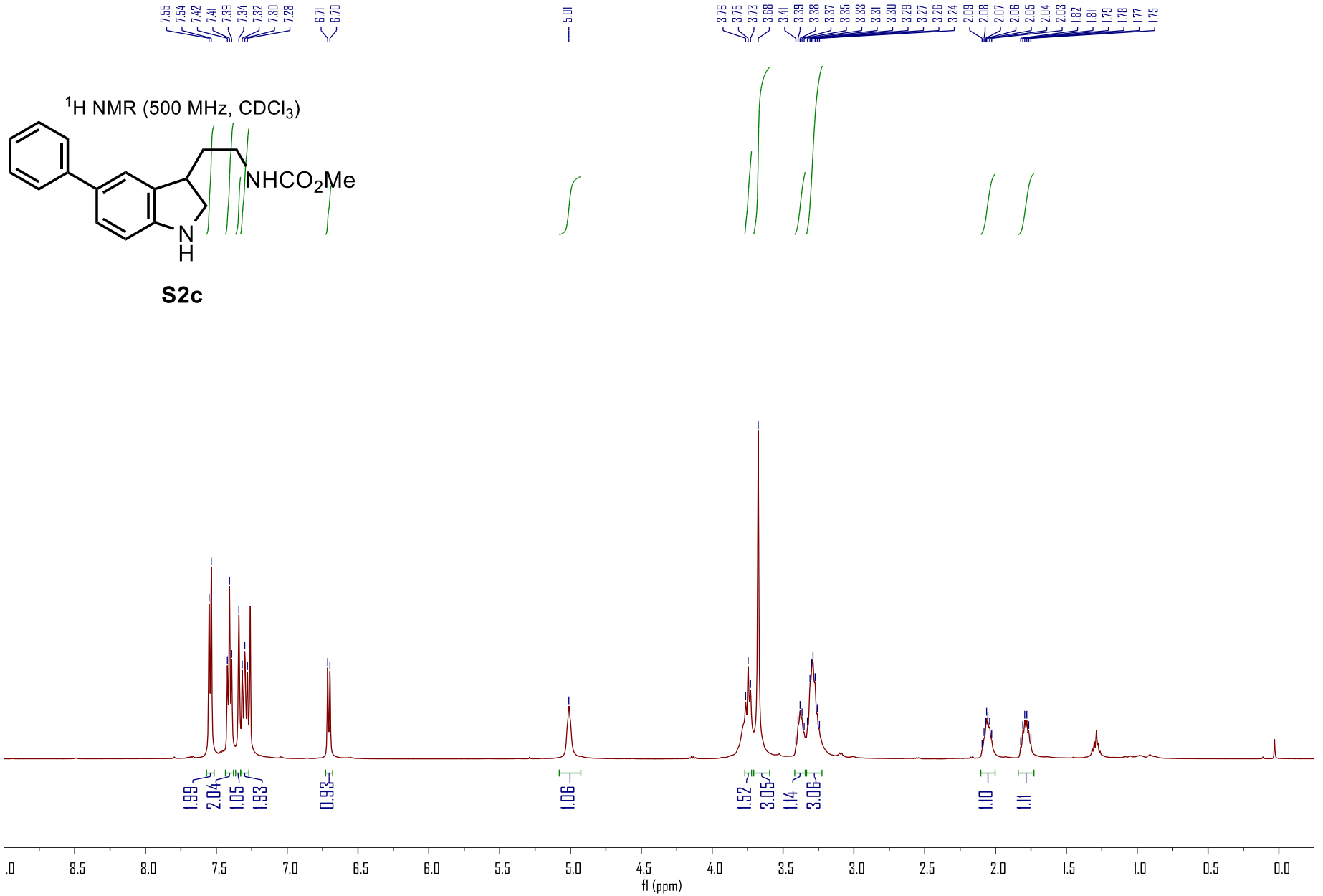


S2b

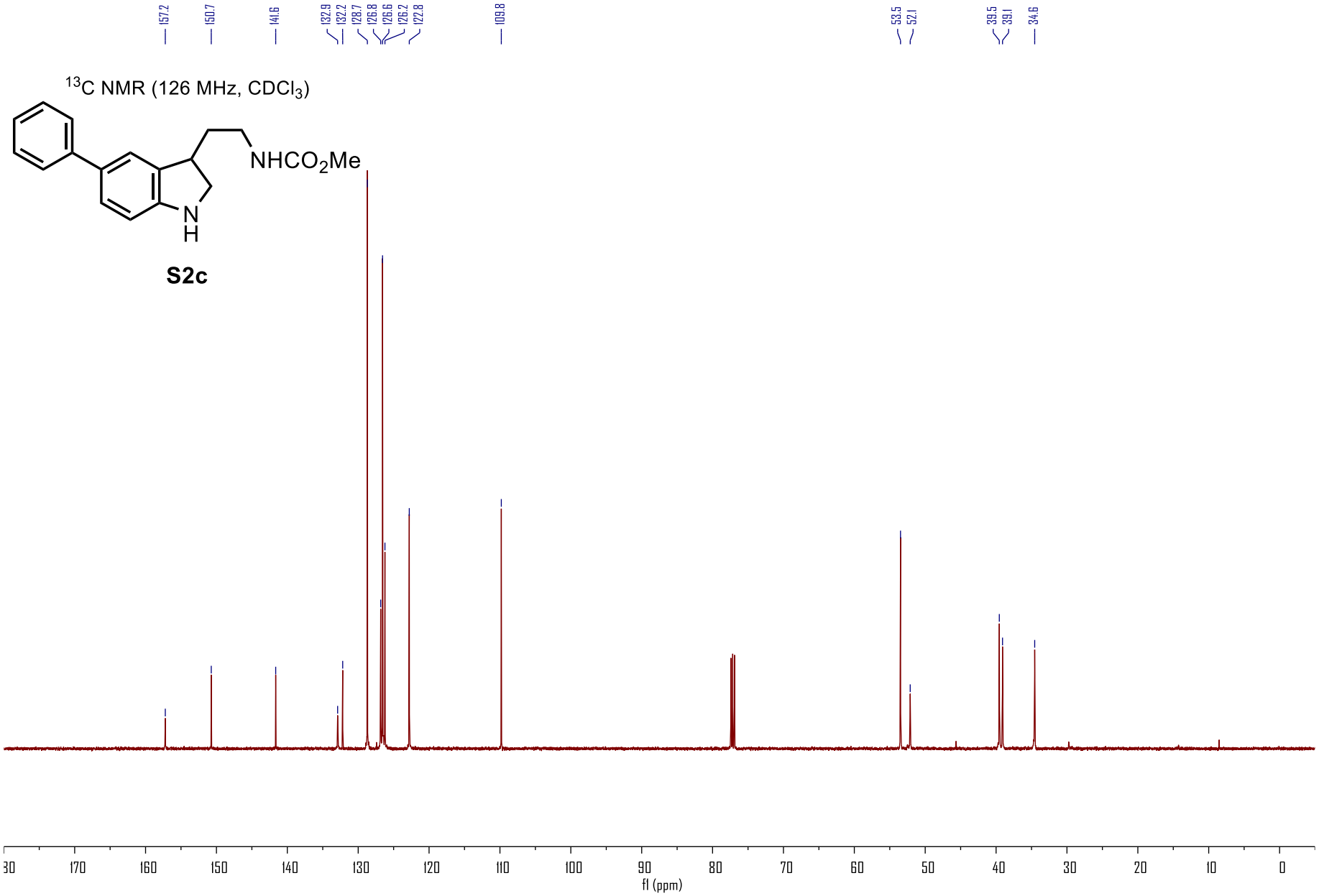

157.2
148.8
132.5
128.1
127.9
124.5
109.7
53.4
51.9
39.5
39.0
34.3
20.8
^{13}C NMR (101 MHz, $CDCl_3$)
Me
NHCO$_2$Me
N
H
f1 (ppm)

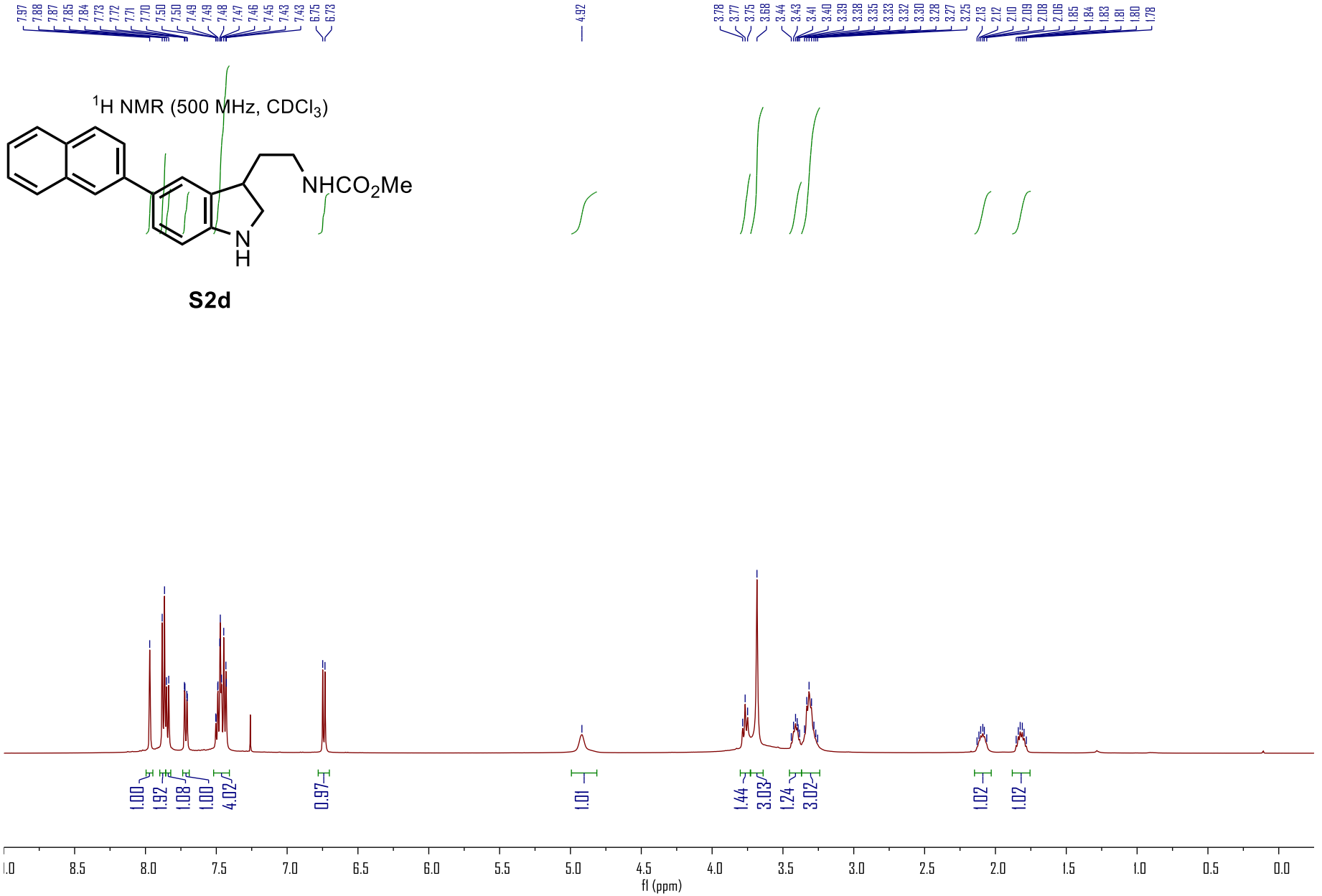
S2b



^{1}H NMR (500 MHz, $CDCl_3$)

S2c


157.2
150.7
141.6
132.9
132.2
128.7
126.8
126.6
126.2
122.8
109.8
53.5
52.1
39.5
39.1
34.6
^{13}C NMR (126 MHz, $CDCl_3$)
NHCO$_2$Me
N
H
S2c
f1 (ppm)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7.87
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7.84
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7.71
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7.50
7.49
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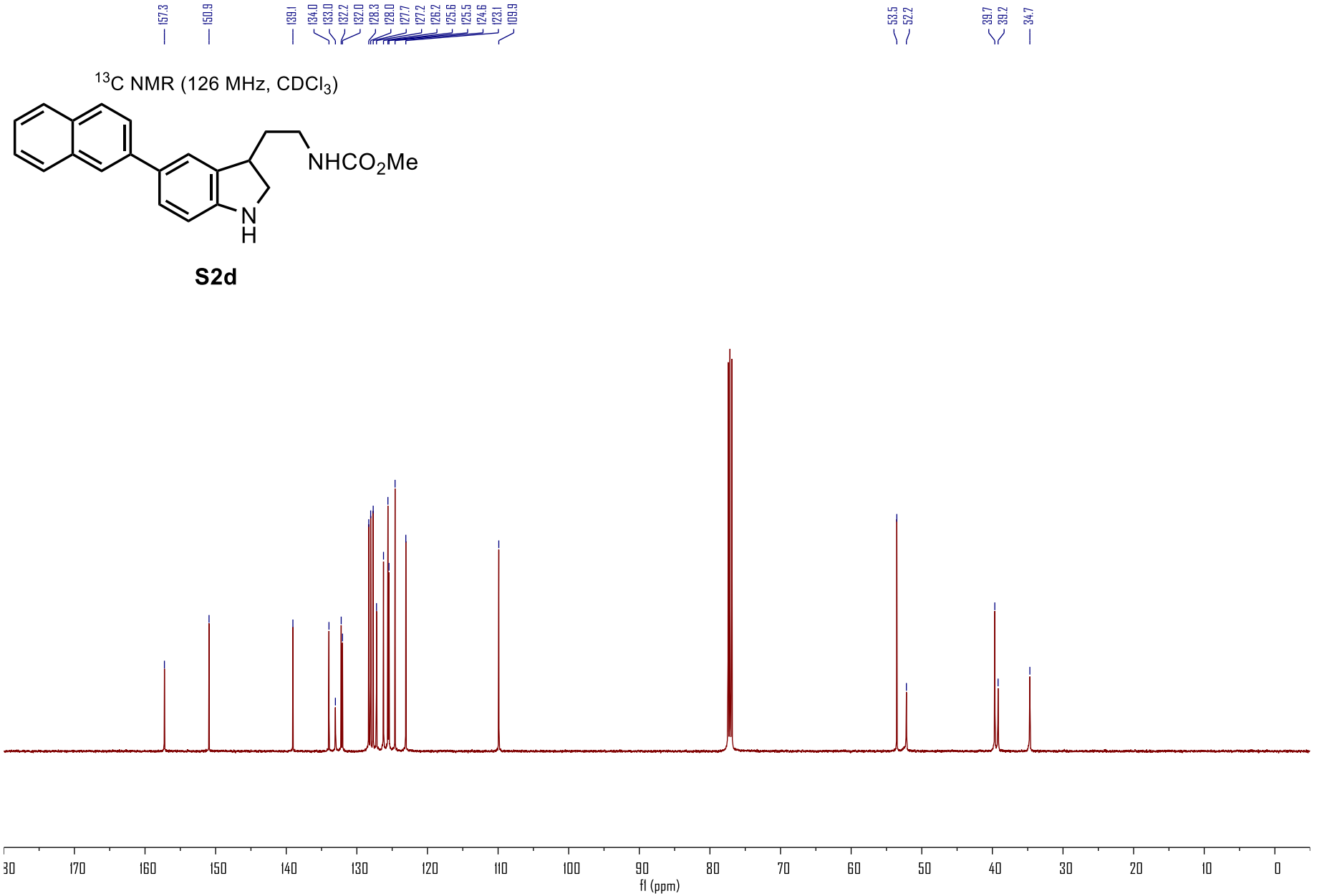
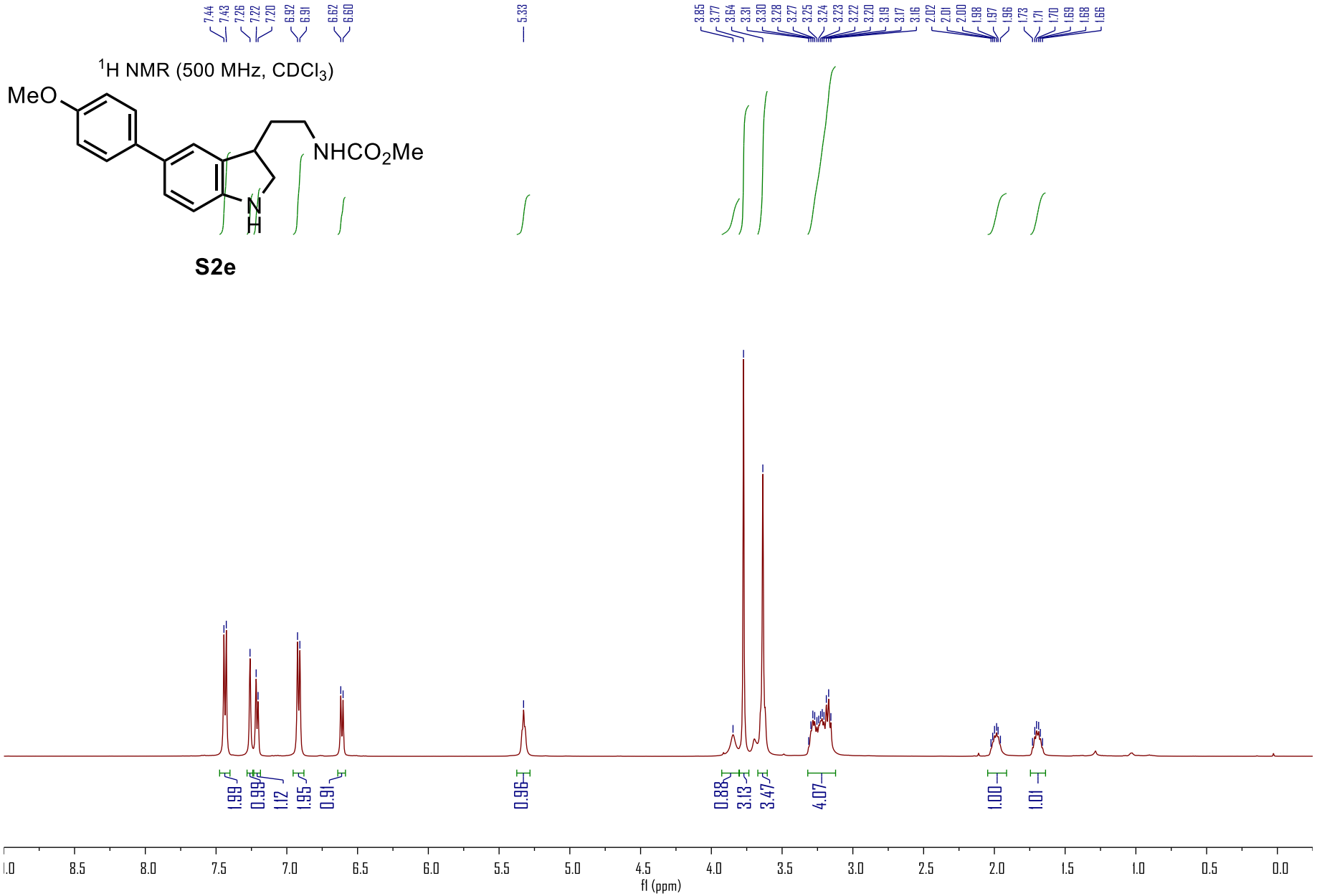
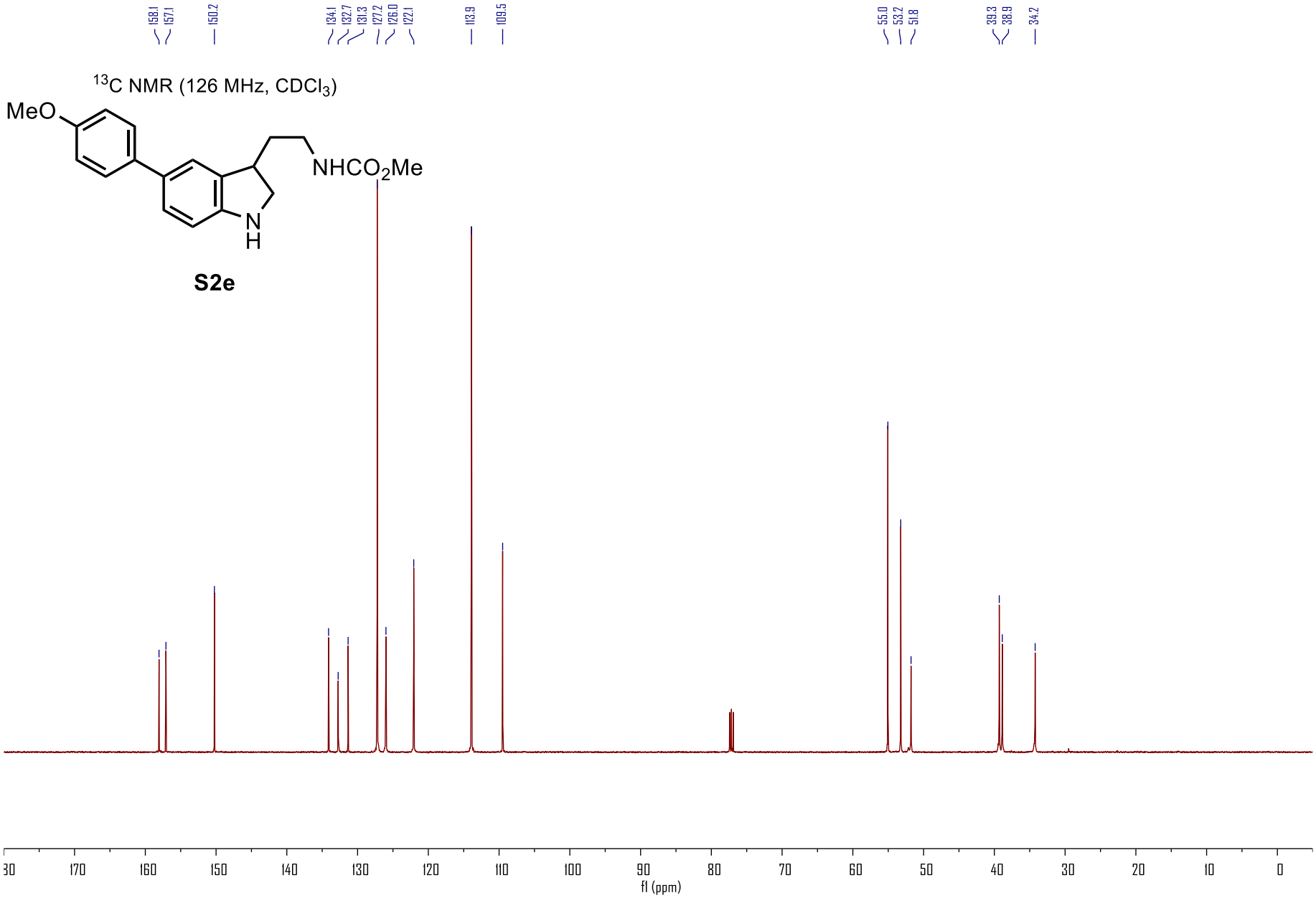
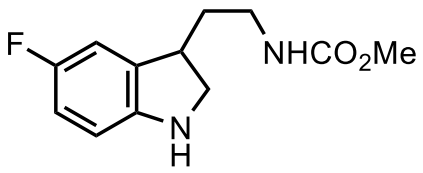
7.48
7.47
7.46
7.45
7.43
7.43
6.75
6.73
4.92
3.78
3.77
3.75
3.68
3.44
3.43
3.41
3.40
3.39
3.38
3.35
3.33
3.32
3.30
3.28
3.27
3.25
2.13
2.12
2.10
2.09
2.08
2.06
1.85
1.84
1.83
1.81
1.80
1.78
1H NMR (500 MHz, CDCl3)
NHCO2Me
N
H
S2d
1.00
1.92
1.08
1.00
4.02
0.97
1.01
1.44
3.03
1.24
3.02
1.02
1.02
f1 (ppm)


157.3
150.9
139.1
134.0
133.0
132.2
132.0
128.3
128.0
127.7
127.2
126.2
125.6
125.5
124.6
123.1
109.9
53.5
52.2
39.7
39.2
34.7
13C NMR (126 MHz, CDCl3)
NHCO2Me
N
H
S2d
f1 (ppm)

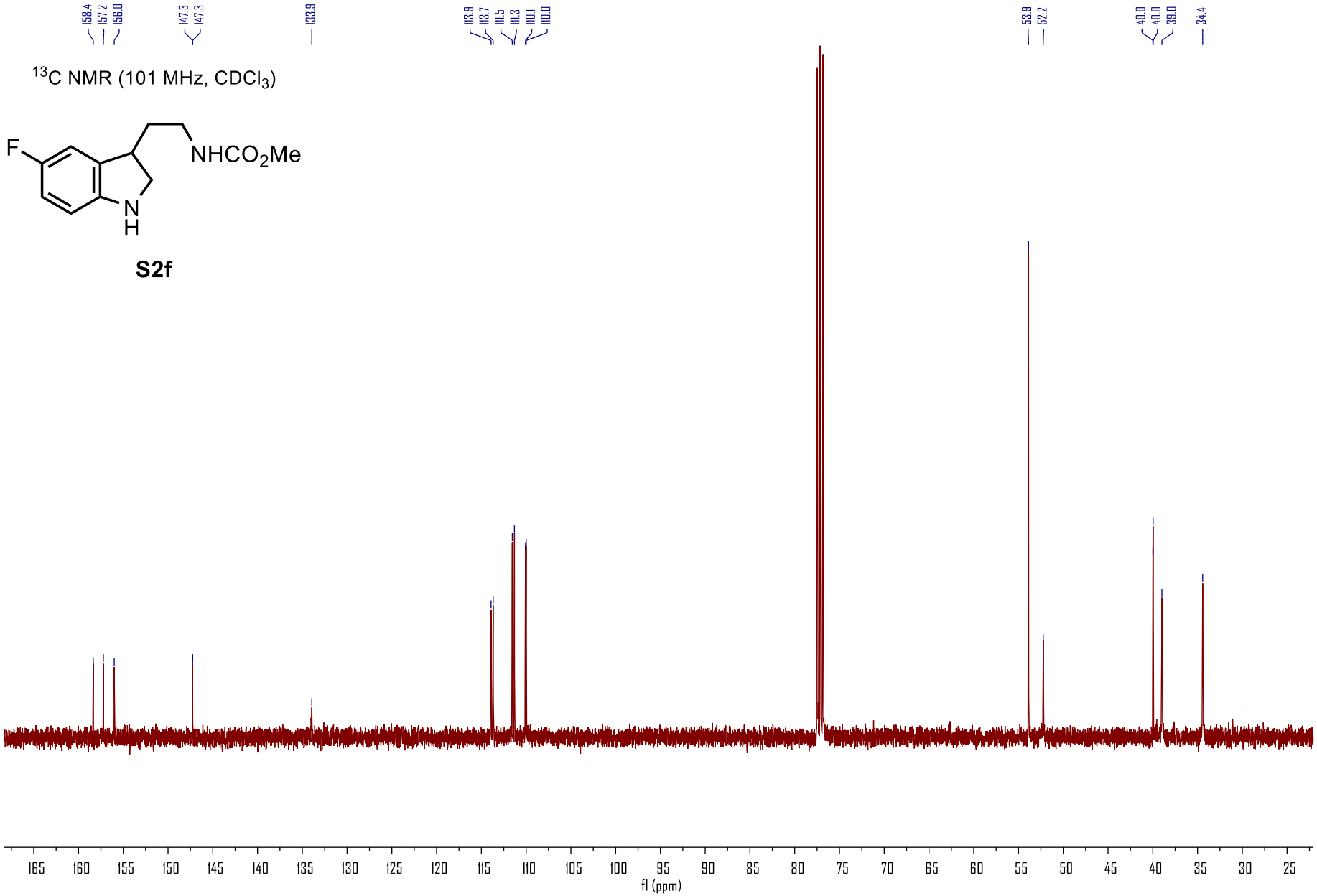

7.44
7.43
7.26
7.22
7.20
6.92
6.91
6.62
6.60
5.33
3.85
3.77
3.64
3.31
3.30
3.28
3.27
3.25
3.24
3.23
3.22
3.20
3.19
3.17
3.16
2.02
2.01
2.00
1.98
1.97
1.96
1.73
1.71
1.70
1.69
1.68
1.66
1H NMR (500 MHz, CDCl3)
MeO
NHCO2Me
N
H
S2e
1.99
0.99
1.12
1.95
0.91
0.96
0.88
3.13
3.47
4.07
1.00
1.01
f1 (ppm)


158.1
157.1
150.2
134.1
132.7
131.3
127.2
126.0
122.1
113.9
109.5
55.0
53.2
51.8
39.3
38.9
34.2
^{13}C NMR (126 MHz, $CDCl_3$)
MeO
NHCO$_2$Me
N
H
S2e
f1 (ppm)

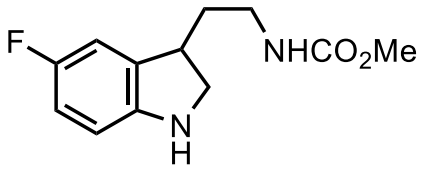
^{1}H NMR (400 MHz, $CDCl_3$)



S2f

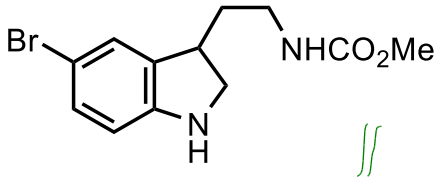

158.4
157.2
156.0
147.3
147.3
133.9
113.9
113.7
111.5
111.3
110.1
110.0
53.9
52.2
40.0
40.0
39.0
34.4
^{13}C NMR (101 MHz, $CDCl_3$)
F
NHCO$_2$Me
N
H
S2f
165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)



S2f

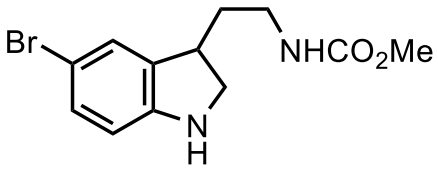
^{1}H NMR (400 MHz, $CDCl_3$)



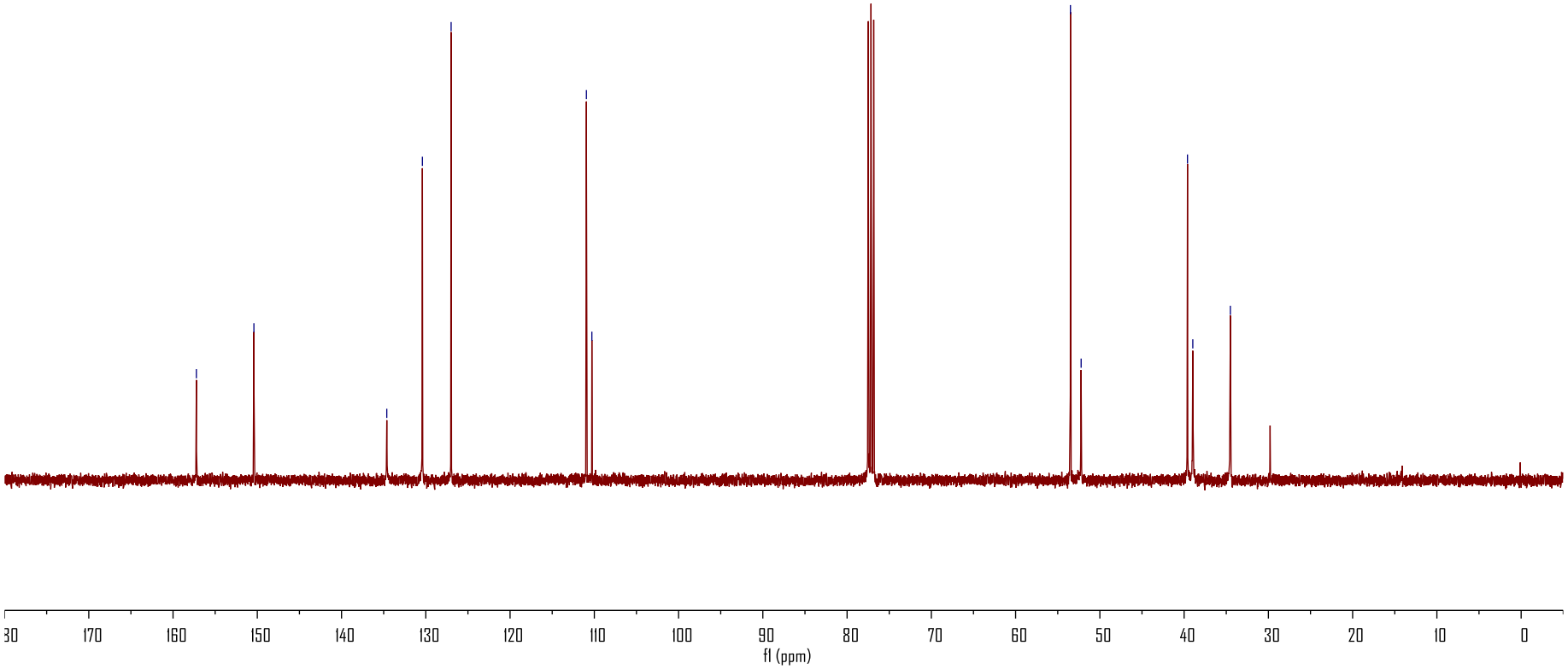
S2g

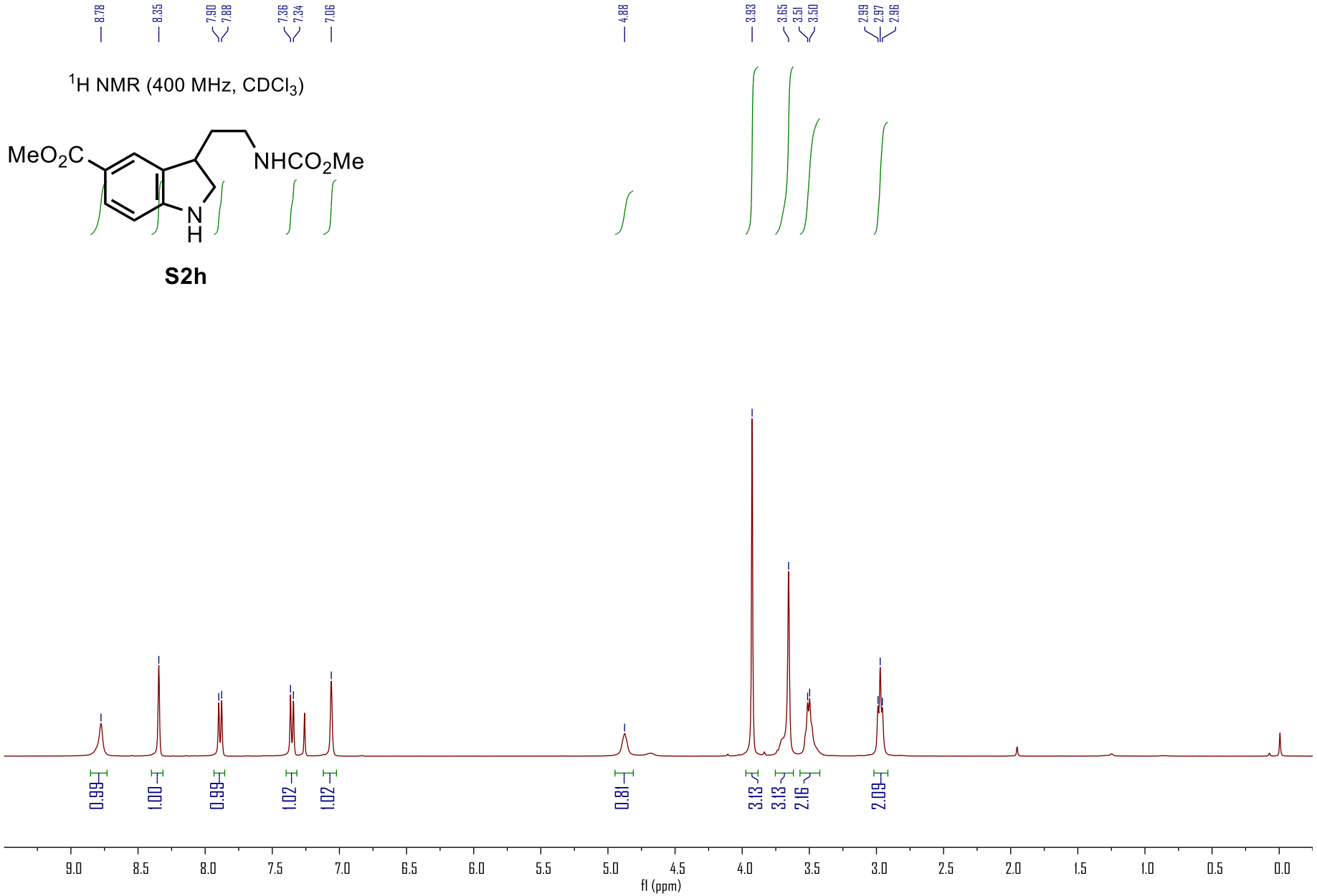
157.2
150.4
134.6
130.4
127.0
110.9
110.3
53.5
52.2
39.6
39.0
34.5

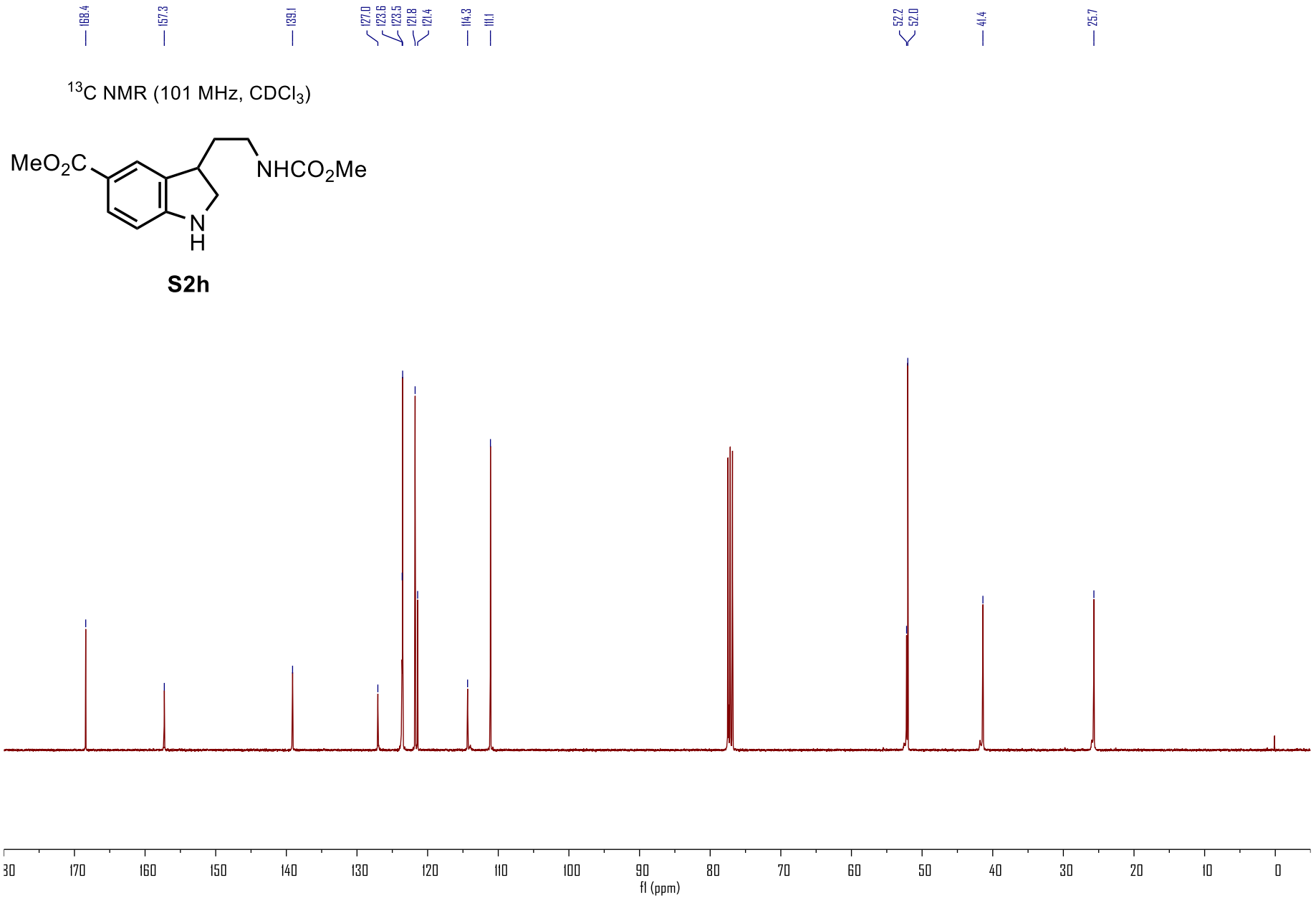
^{13}C NMR (101 MHz, $CDCl_3$)



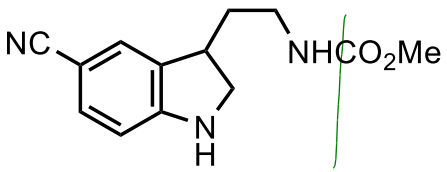
S2g



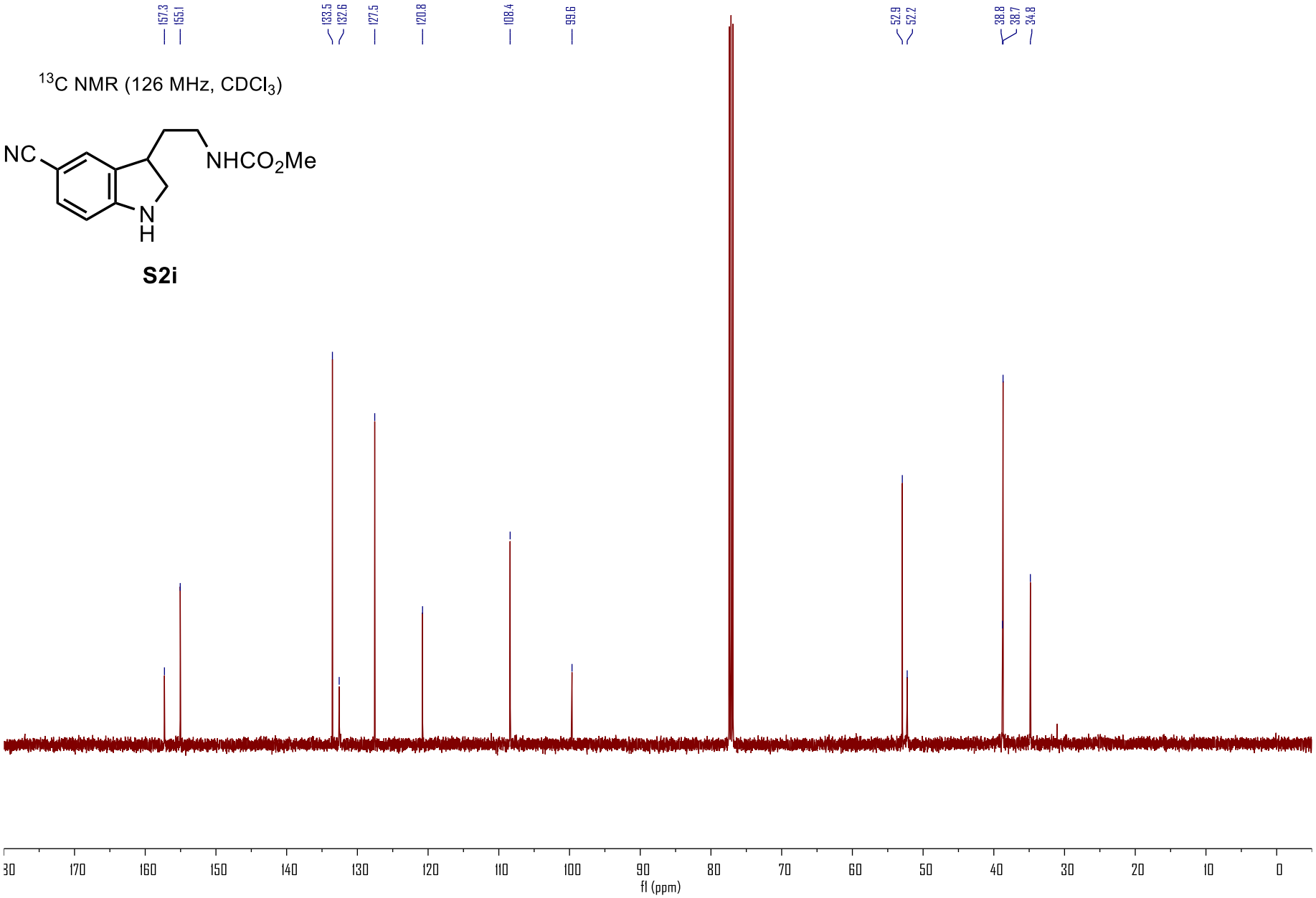

8.78
8.35
7.90
7.88
7.36
7.34
7.06
4.88
3.93
3.65
3.51
3.50
2.99
2.97
2.96
^{1}H NMR (400 MHz, $CDCl_3$)
MeO_2C
$NHCO_2Me$
N
H
S2h
0.99
1.00
0.99
1.02
1.02
0.81
3.13
3.13
2.16
2.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


168.4
157.3
139.1
127.0
123.6
123.5
121.8
121.4
114.3
111.1
52.2
52.0
41.4
25.7
MeO2C
NHCO2Me
N
H
S2h
13C NMR (101 MHz, CDCl3)
f1 (ppm)

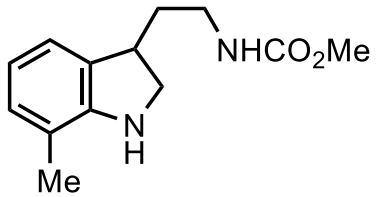
^{1}H NMR (500 MHz, MeOD)



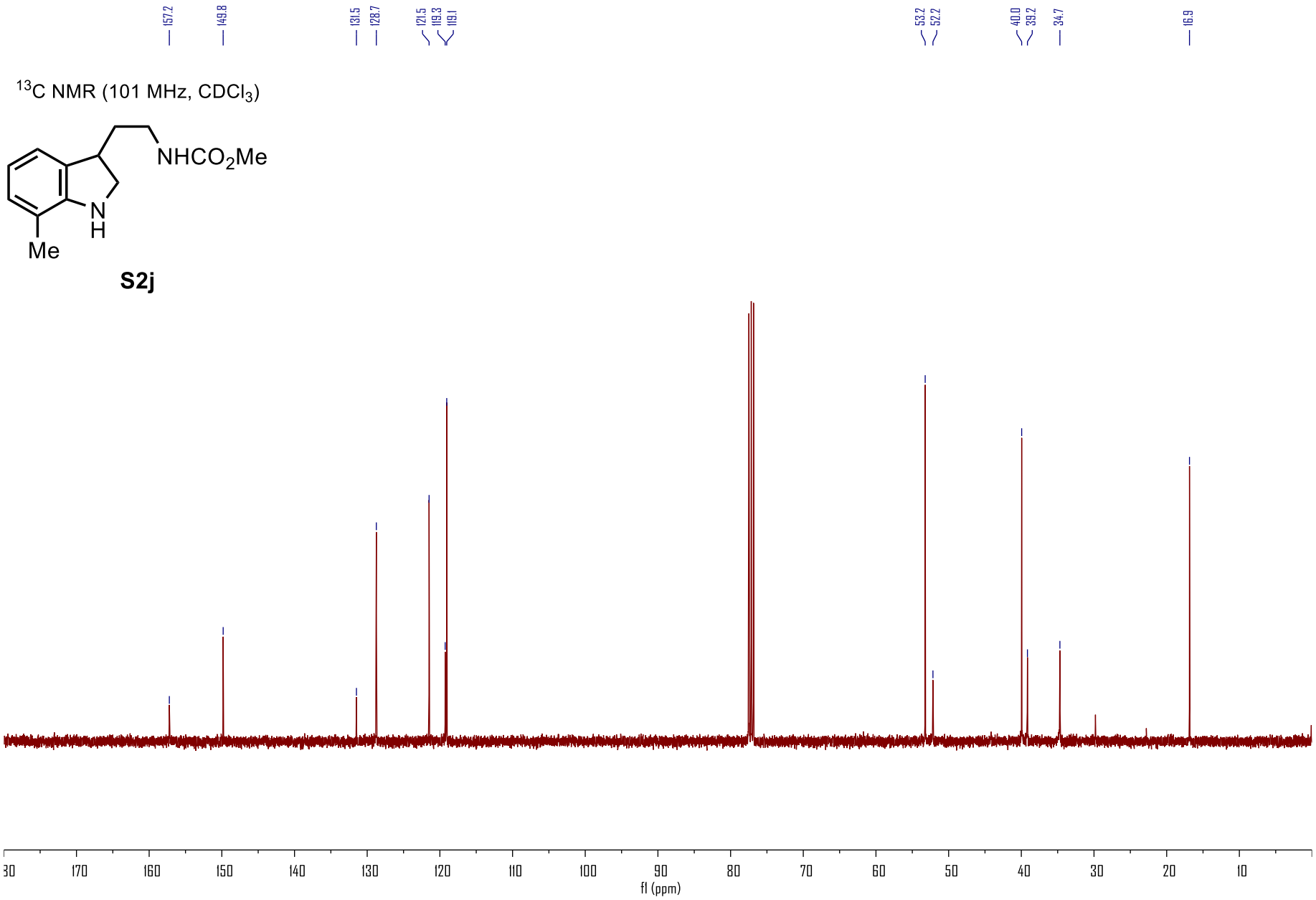
S2i


157.3
155.1
133.5
132.6
127.5
120.8
108.4
99.6
52.9
52.2
38.8
38.7
34.8
^{13}C NMR (126 MHz, $CDCl_3$)
NC
$NHCO_2Me$
N
H
S2i
f1 (ppm)

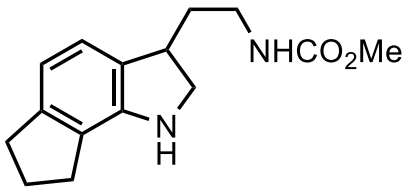
^{1}H NMR (400 MHz, $CDCl_3$)



S2j

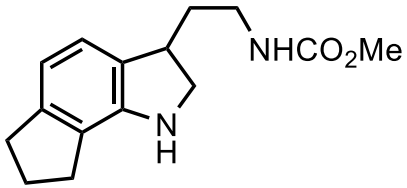

157.2
149.8
131.5
128.7
121.5
119.3
119.1
53.2
52.2
40.0
39.2
34.7
16.9
^{13}C NMR (101 MHz, $CDCl_3$)
NHCO$_2$Me
N
H
Me
S2j
f1 (ppm)

^{1}H NMR (500 MHz, $CDCl_3$)



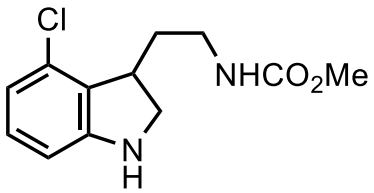
S2k

^{13}C NMR (126 MHz, $CDCl_3$)

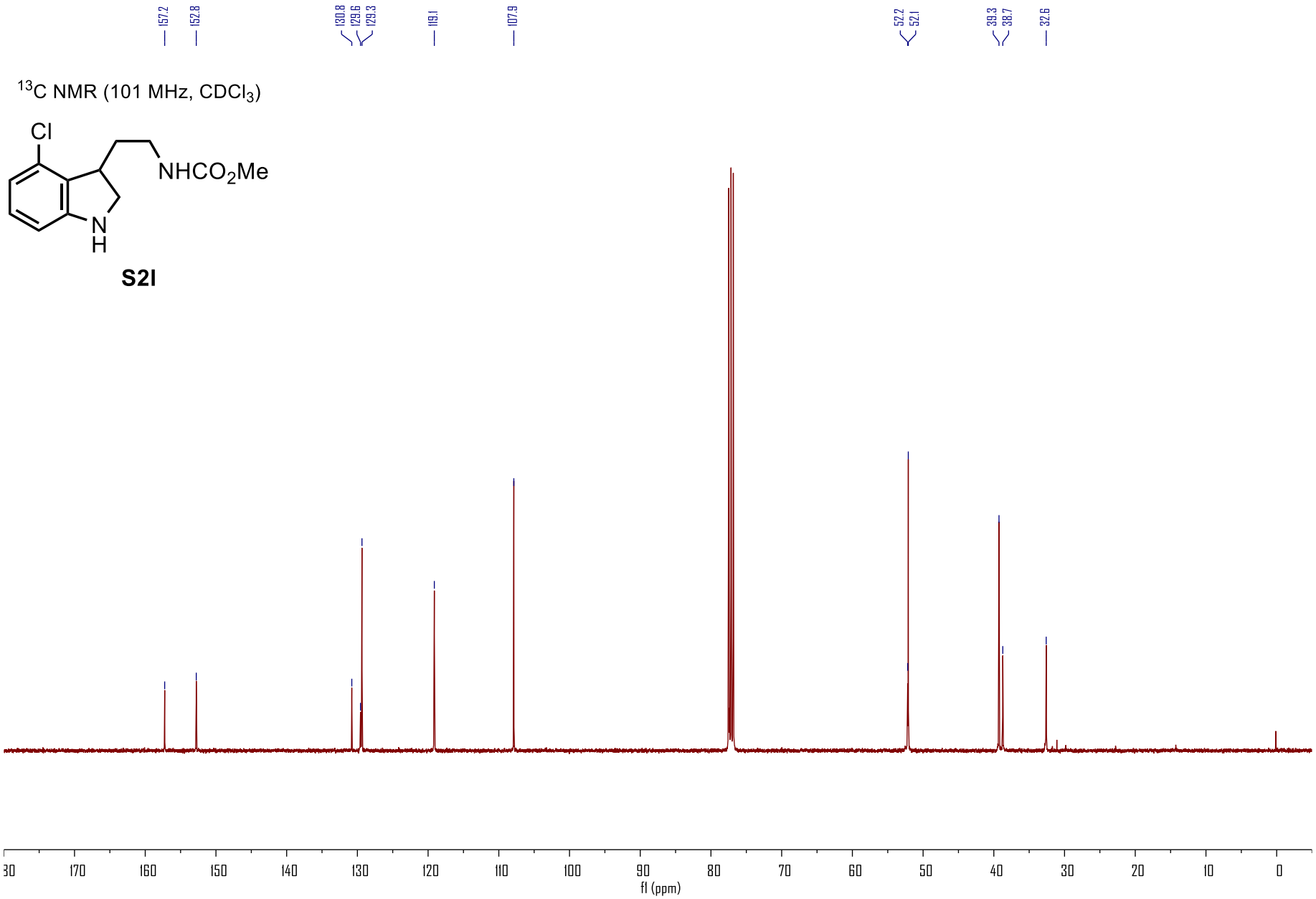


S2k

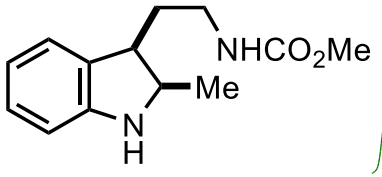
^{1}H NMR (400 MHz, $CDCl_3$)



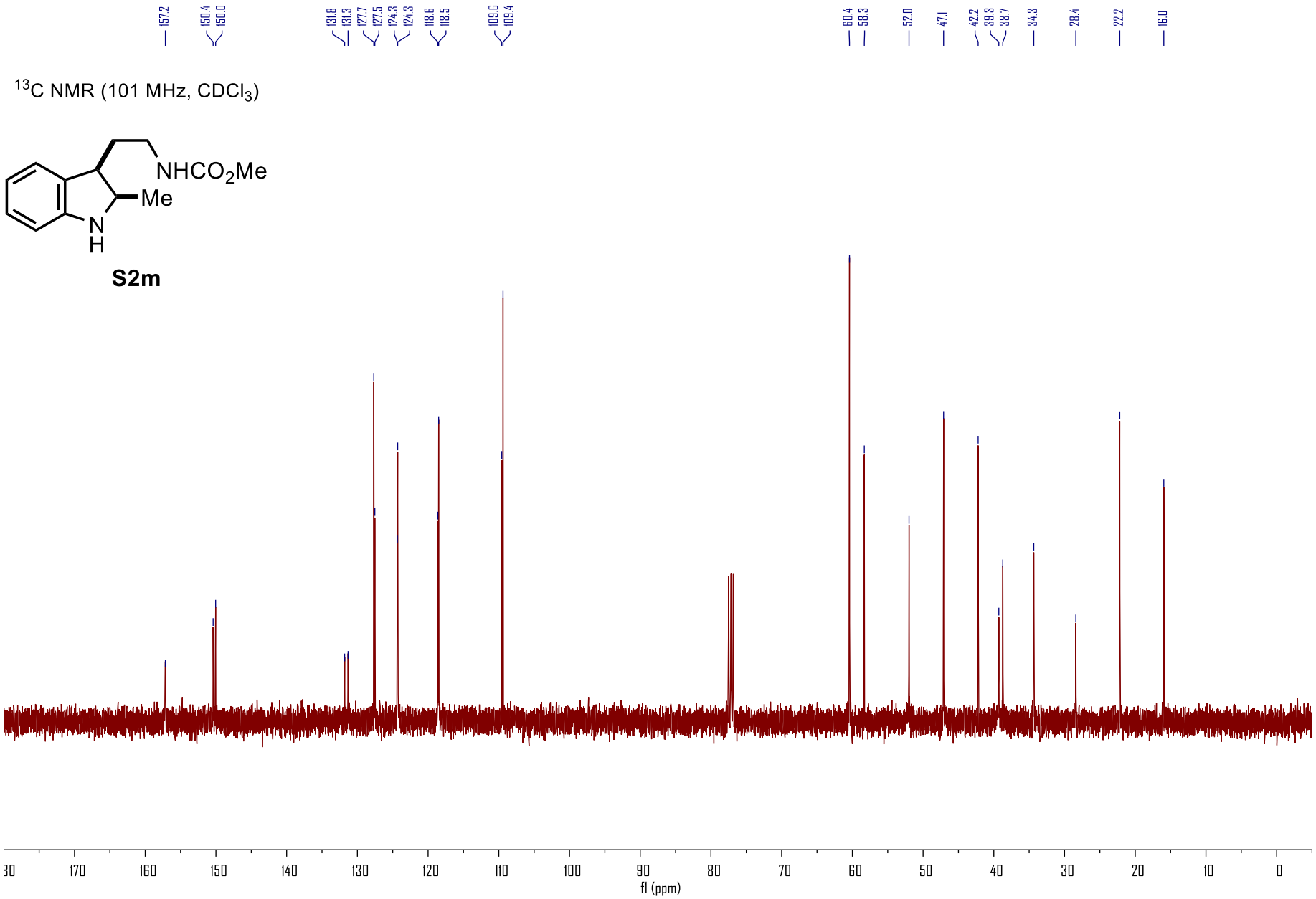
S2l

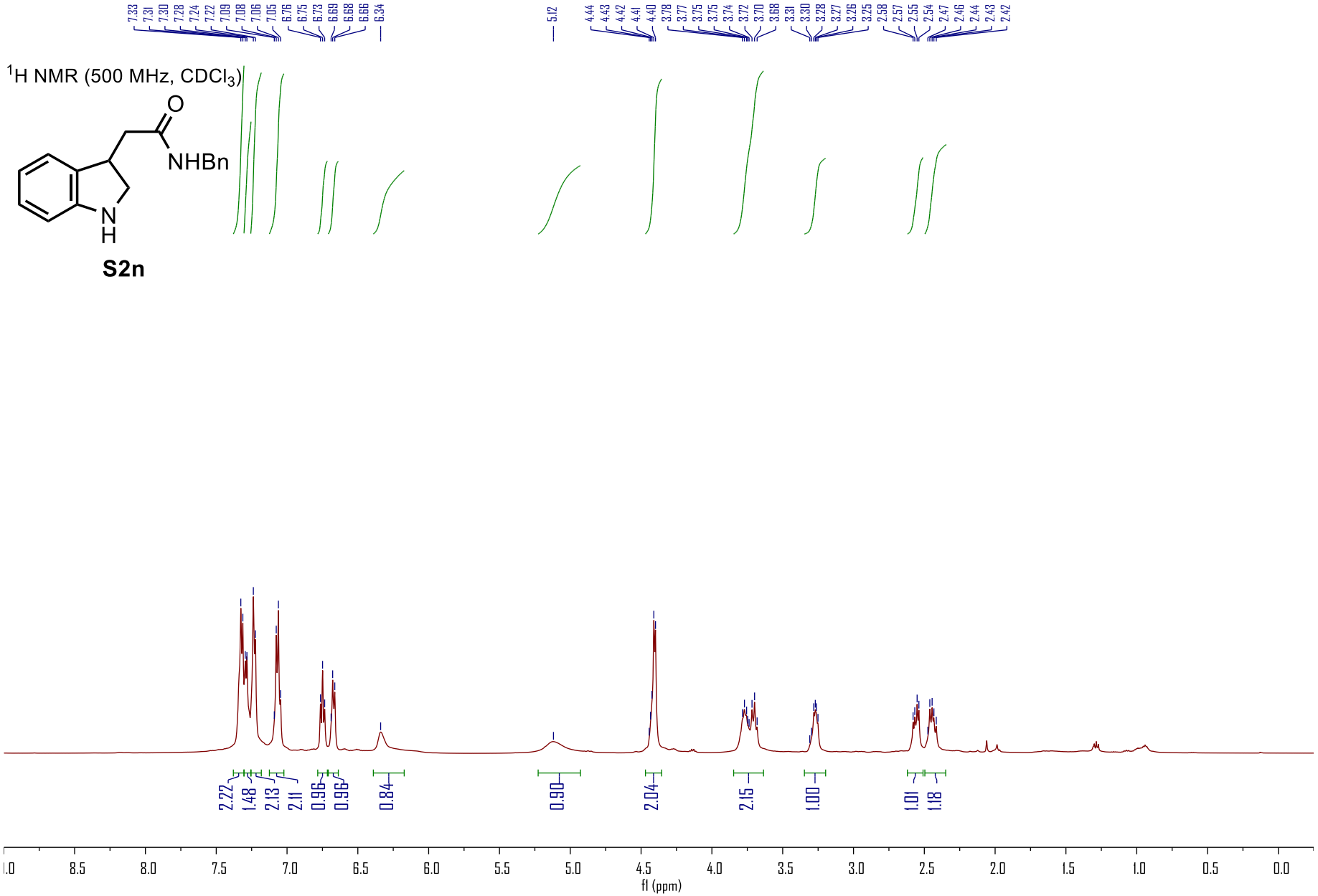

157.2
152.8
130.8
129.6
129.3
119.1
107.9
52.2
52.1
39.3
38.7
32.6
^{13}C NMR (101 MHz, $CDCl_3$)
Cl
$NHCO_2Me$
N
H
S2l
f1 (ppm)

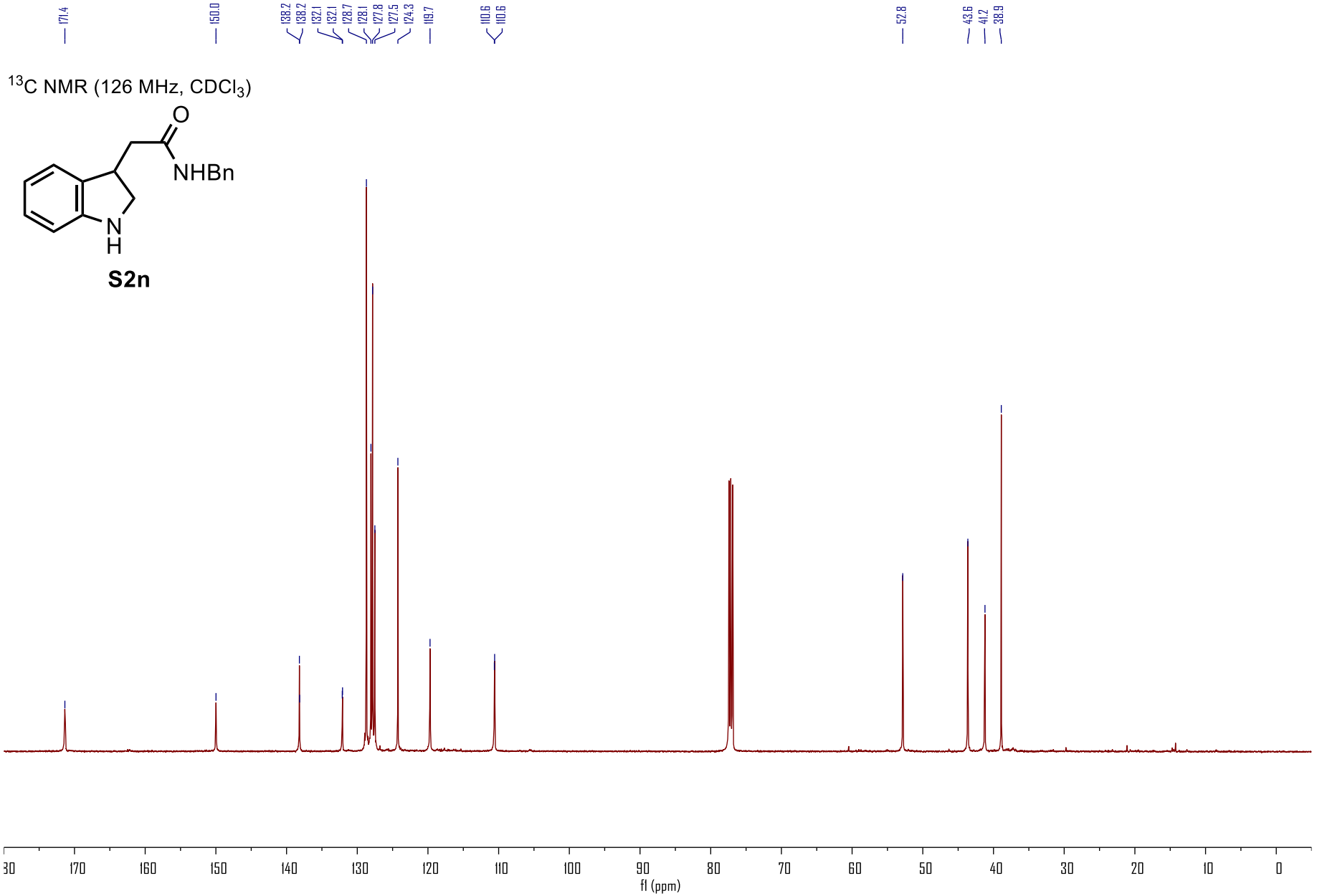
^{1}H NMR (400 MHz, $CDCl_3$)

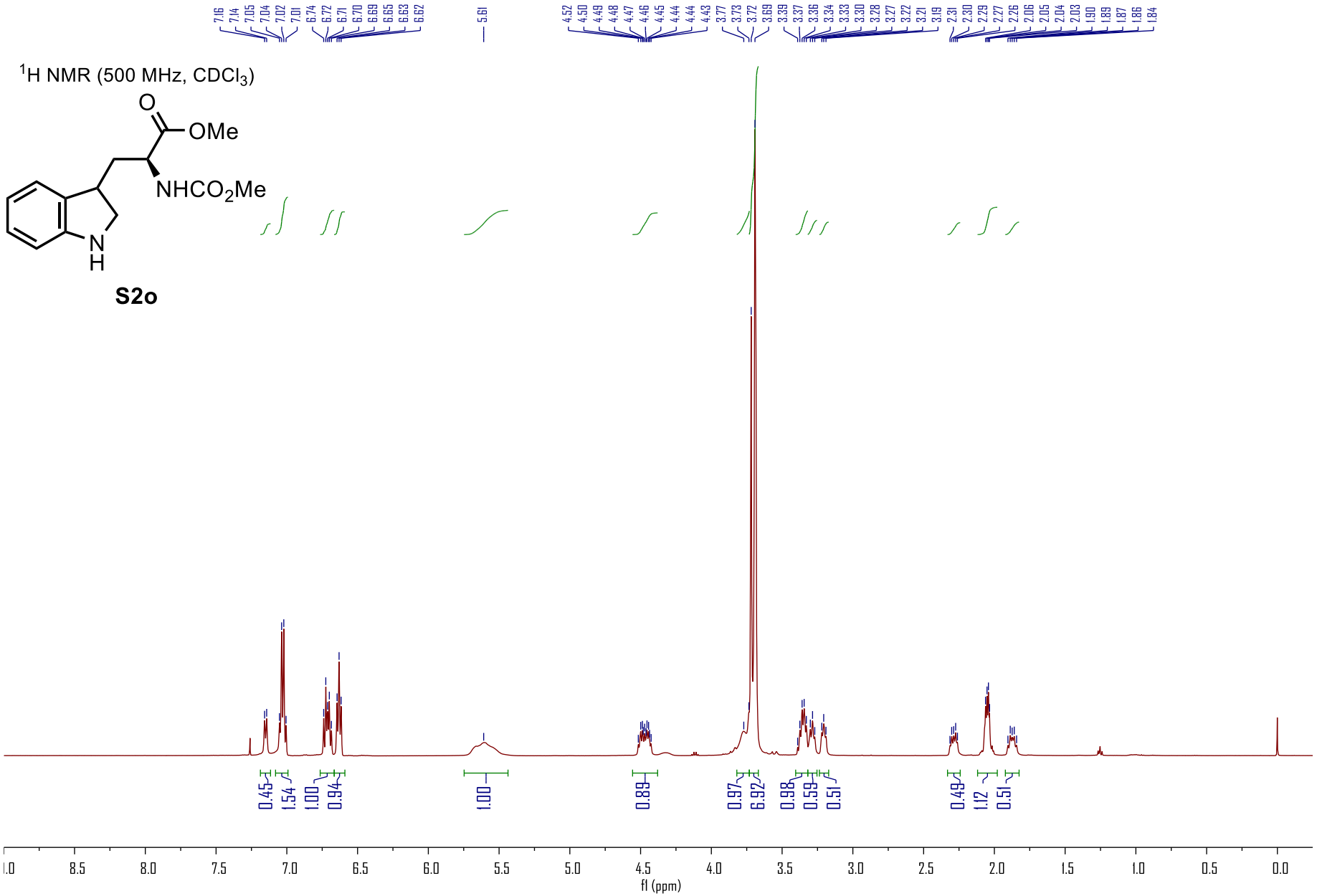


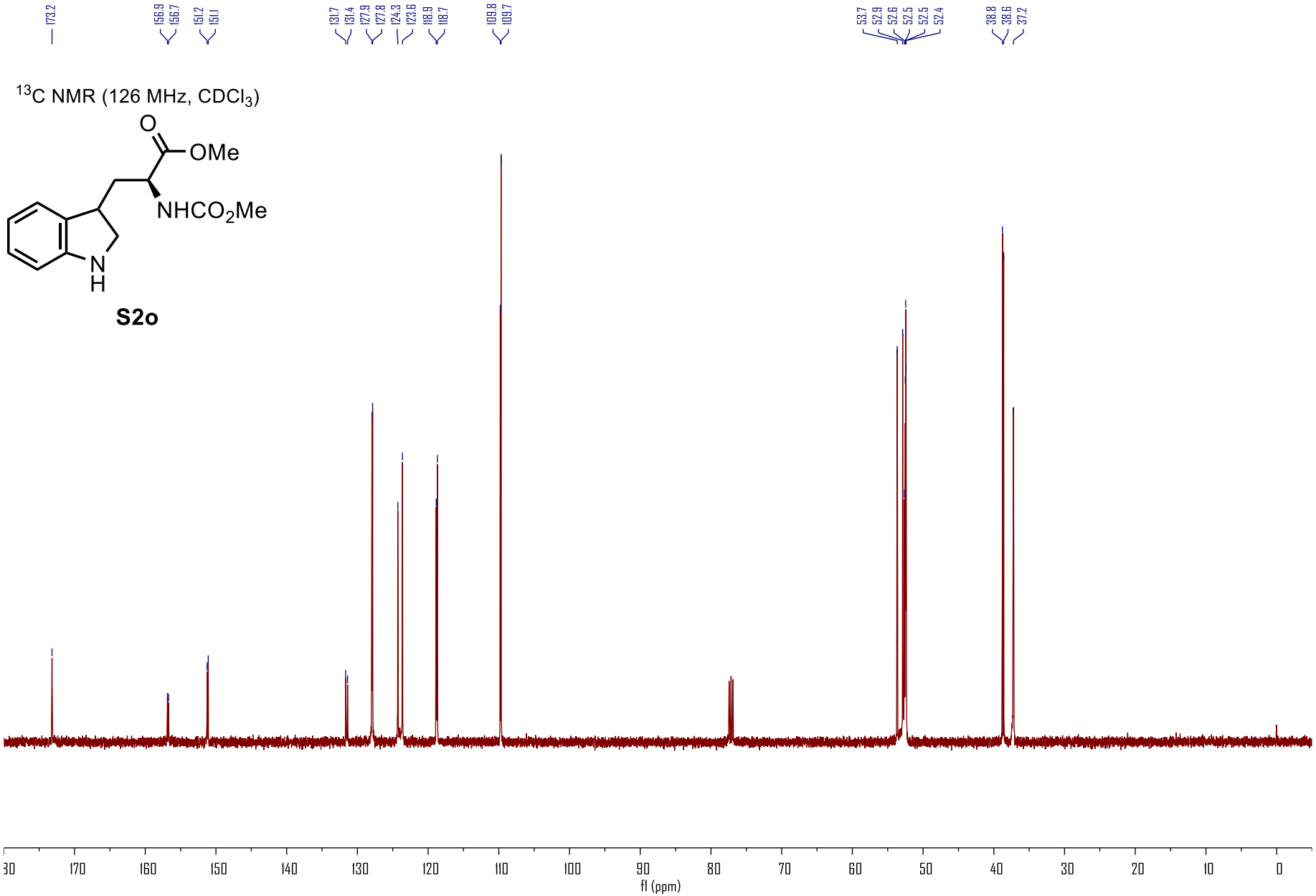
S2m


157.2
150.4
150.0
131.8
131.3
127.7
127.5
124.3
124.3
118.6
118.5
109.6
109.4
60.4
58.3
52.0
47.1
42.2
39.3
38.7
34.3
28.4
22.2
16.0
^{13}C NMR (101 MHz, $CDCl_3$)
NHCO$_2$Me
Me
N
H
S2m
f1 (ppm)

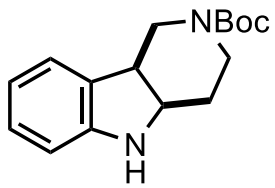

7.33
7.31
7.30
7.28
7.24
7.22
7.09
7.08
7.06
7.05
6.76
6.75
6.73
6.69
6.68
6.66
6.34
5.12
4.44
4.43
4.42
4.41
4.40
3.78
3.77
3.75
3.75
3.74
3.72
3.70
3.68
3.31
3.30
3.28
3.27
3.26
3.25
2.58
2.57
2.55
2.54
2.47
2.46
2.44
2.43
2.42
1H NMR (500 MHz, CDCl3)
O
NHBn
N
H
S2n
2.22
1.48
2.13
2.11
0.96
0.96
0.84
0.90
2.04
2.15
1.00
1.01
1.18
f1 (ppm)


171.4
150.0
138.2
138.2
132.1
132.1
128.7
128.1
127.8
127.5
124.3
119.7
110.6
110.6
52.8
43.6
41.2
38.9
^{13}C NMR (126 MHz, $CDCl_3$)
O
NHBn
N
H
S2n
f1 (ppm)

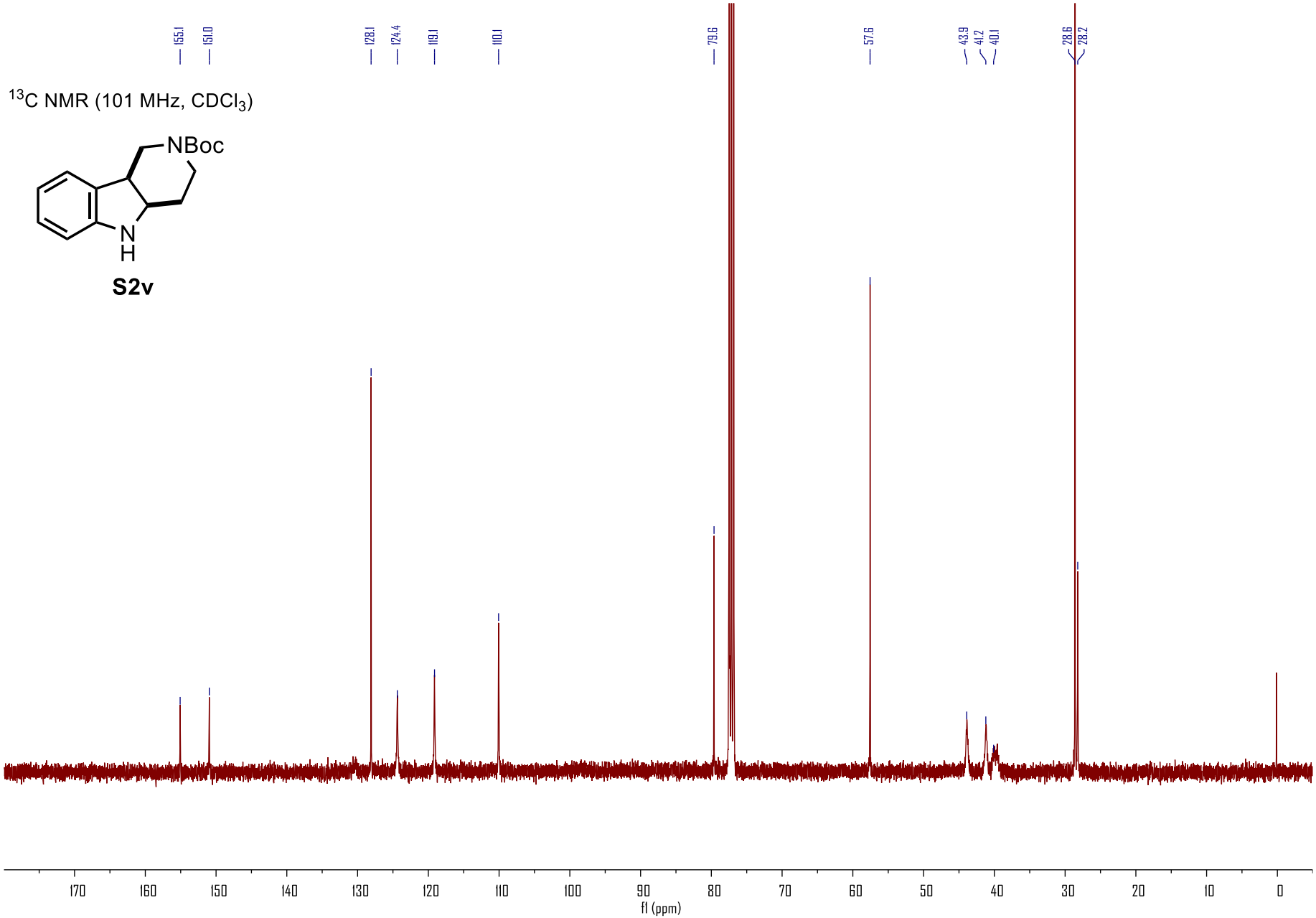

7.16
7.14
7.05
7.04
7.02
7.01
6.74
6.72
6.71
6.70
6.69
6.65
6.63
6.62
5.61
4.52
4.50
4.49
4.48
4.47
4.46
4.45
4.44
4.44
4.43
3.77
3.73
3.72
3.69
3.39
3.37
3.36
3.34
3.33
3.30
3.28
3.27
3.22
3.21
3.19
2.31
2.30
2.29
2.27
2.26
2.06
2.05
2.04
2.03
1.90
1.89
1.87
1.86
1.84
^{1}H NMR (500 MHz, $CDCl_3$)
O
OMe
$NHCO_2Me$
N
H
S2o
0.45
1.54
1.00
0.94
1.00
0.89
0.97
6.92
0.98
0.59
0.51
0.49
1.12
0.51
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


173.2
156.9
155.7
151.2
151.1
131.7
131.4
127.9
127.8
124.3
123.6
118.9
118.7
109.8
109.7
53.7
52.9
52.6
52.5
52.5
52.4
38.8
38.6
37.2
13C NMR (126 MHz, CDCl3)
O
OMe
NHCO2Me
N
H
S2o
f1 (ppm)

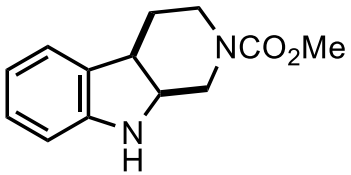
^{1}H NMR (400 MHz, $CDCl_3$)



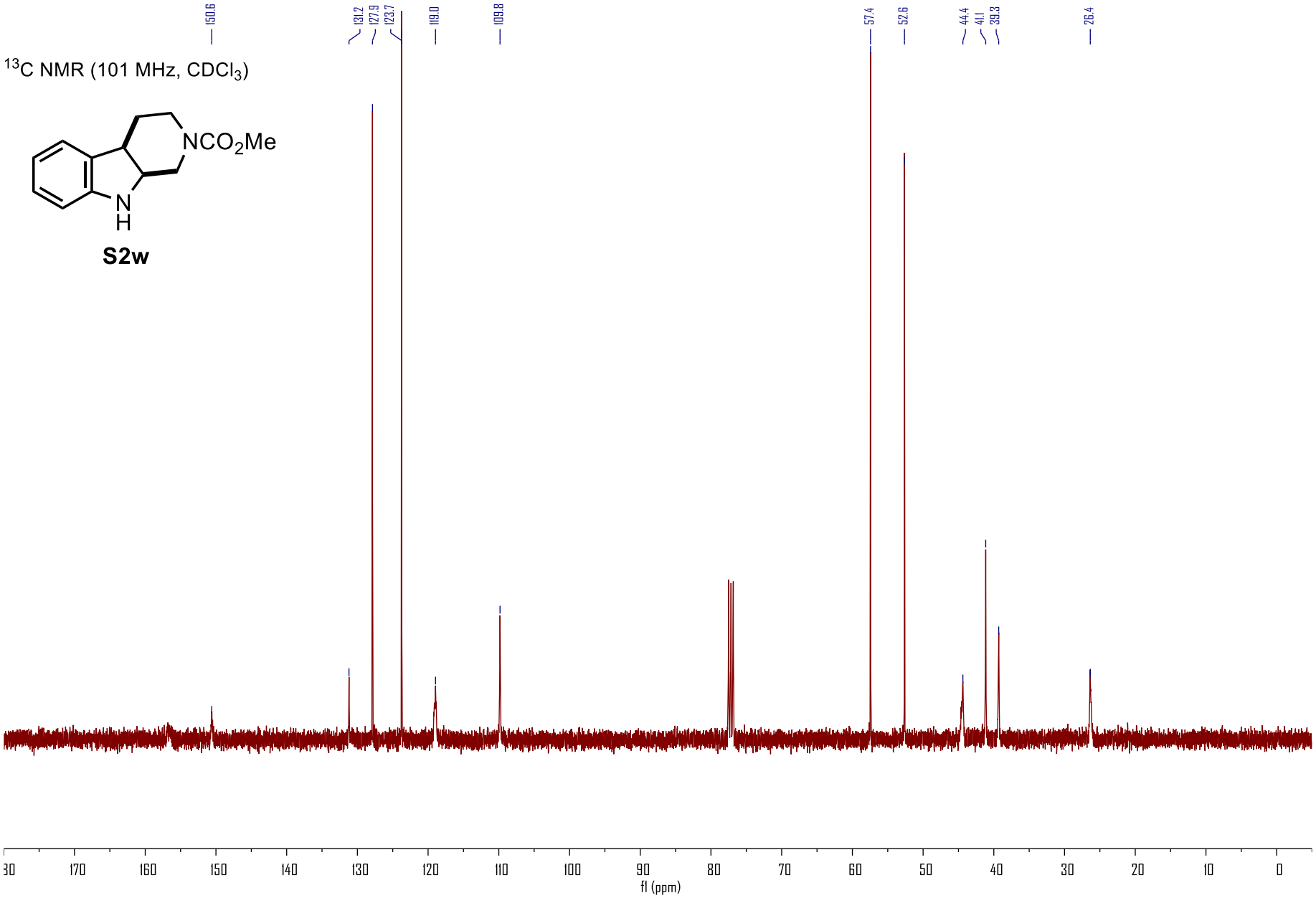
S2v


155.1
151.0
128.1
124.4
119.1
110.1
79.6
57.6
43.9
41.2
40.1
28.6
28.2
^{13}C NMR (101 MHz, $CDCl_3$)
NBoc
N
H
S2v
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

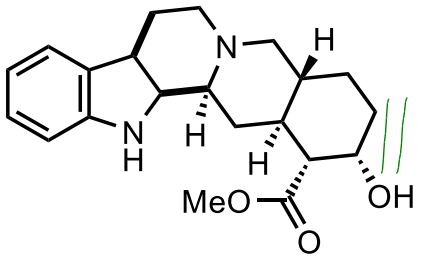
^{1}H NMR (400 MHz, $CDCl_3$)



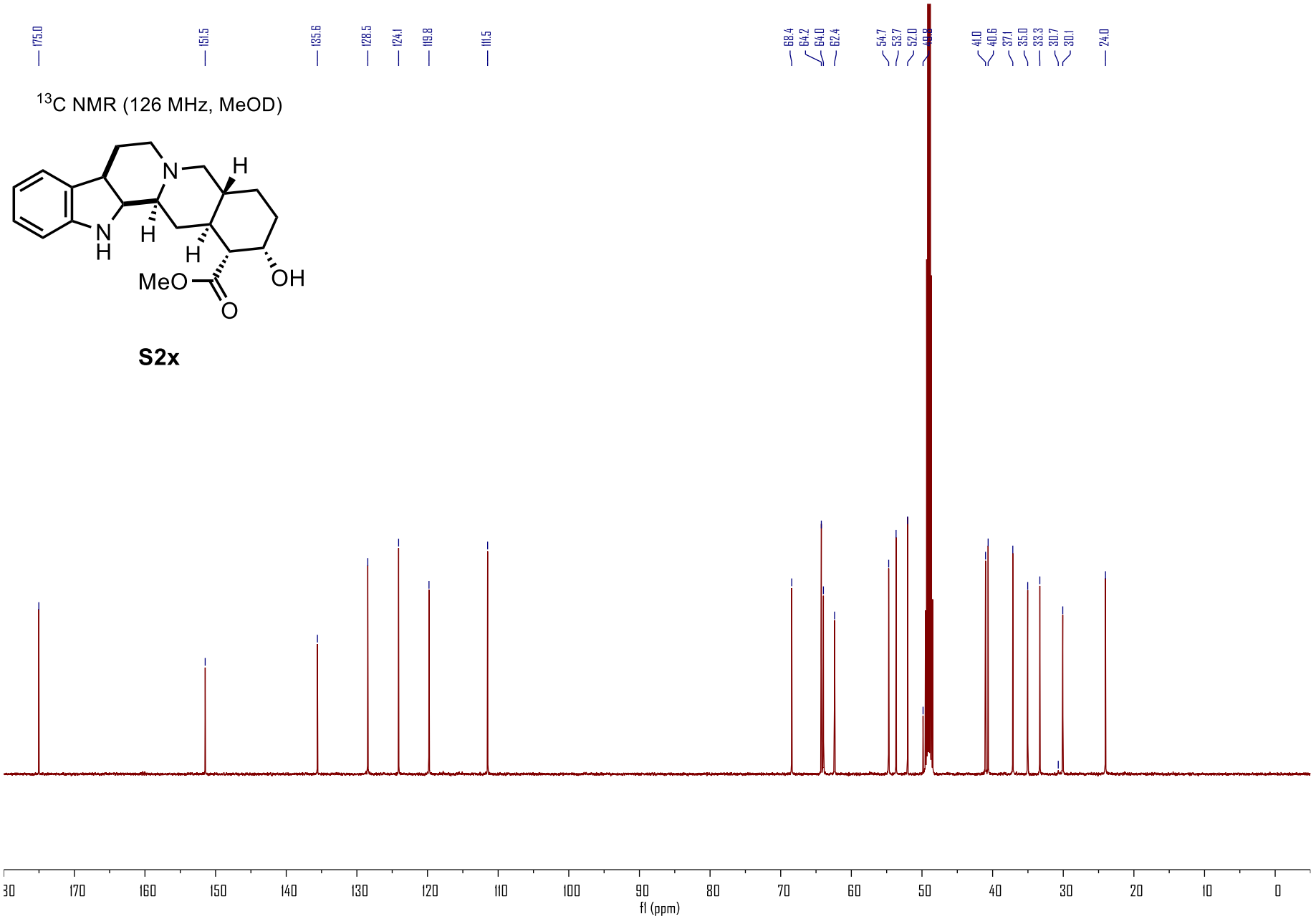
S2w

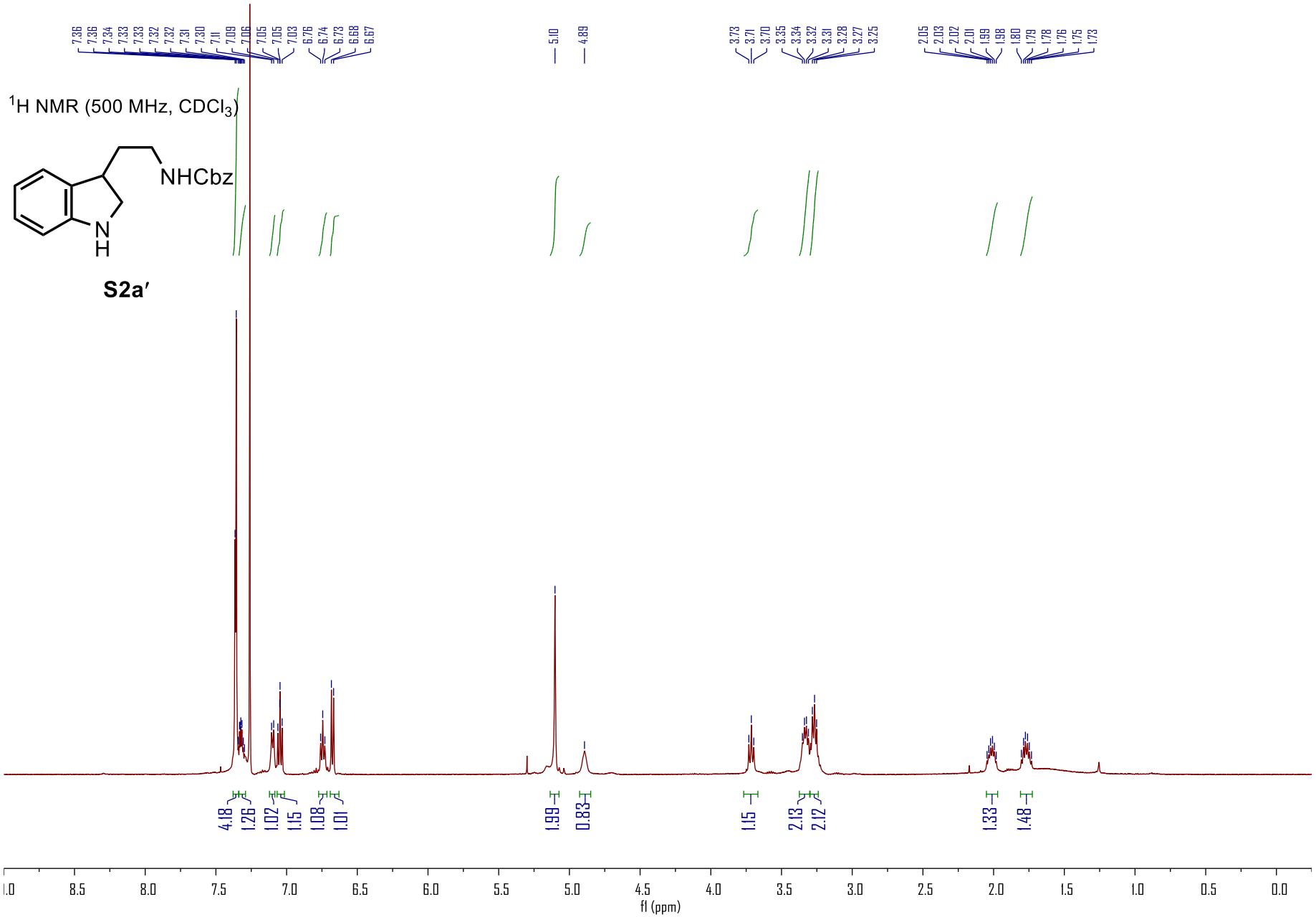

150.6
131.2
127.9
123.7
119.0
109.8
57.4
52.6
44.4
41.1
39.3
26.4
^{13}C NMR (101 MHz, $CDCl_3$)
NCO_2Me
N
H
S2w
f1 (ppm)

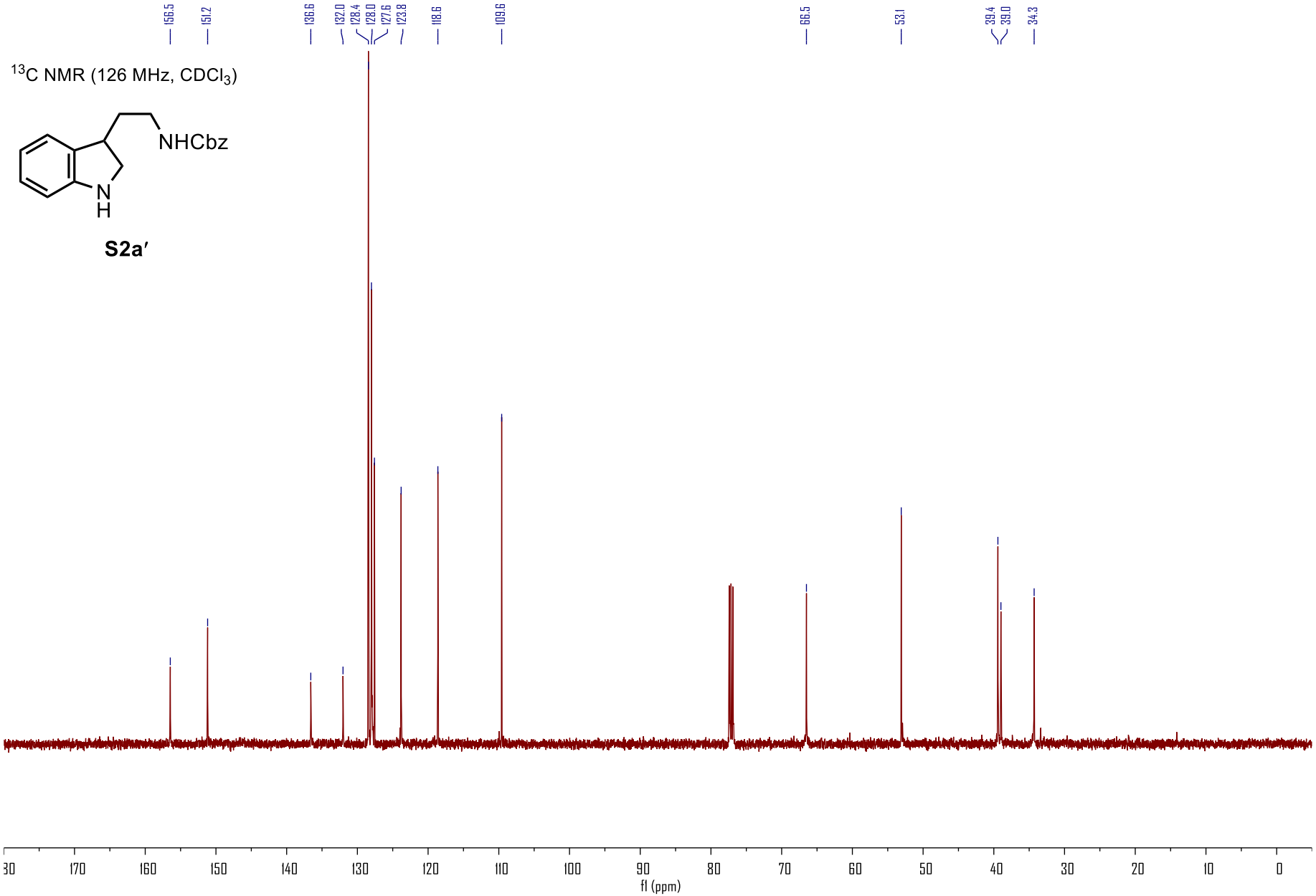
^{1}H NMR (500 MHz, MeOD)



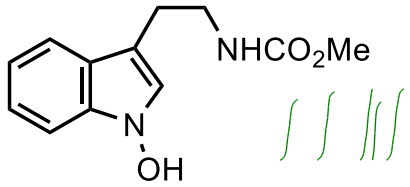
S2x


175.0
151.5
135.6
128.5
124.1
119.8
111.5
68.4
64.2
64.0
62.4
54.7
53.7
52.0
41.0
40.6
37.1
35.0
33.3
30.7
30.1
24.0
13C NMR (126 MHz, MeOD)
N
H
H
H
H
N
MeO
O
OH
S2x
f1 (ppm)

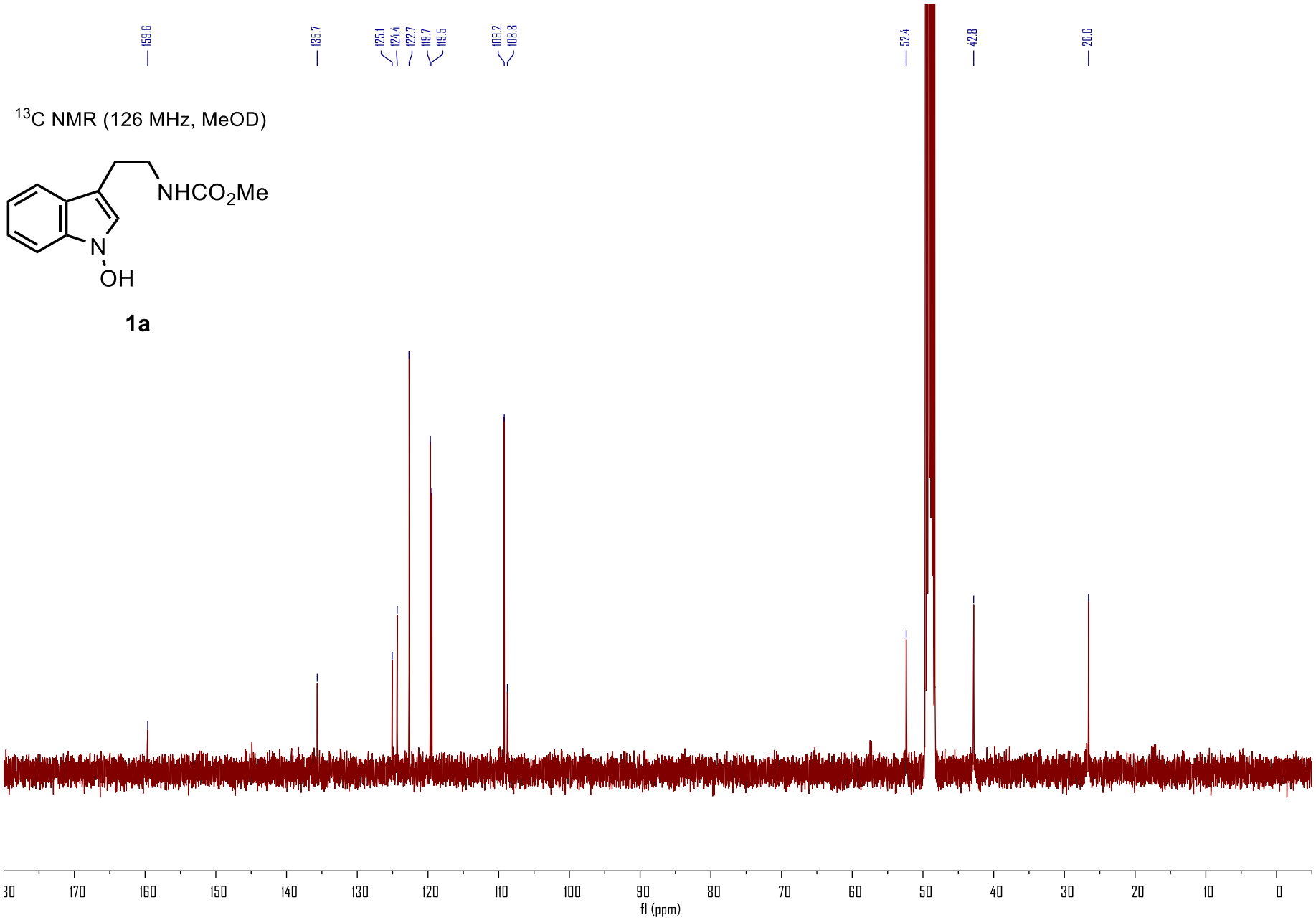

7.38
7.36
7.34
7.33
7.33
7.32
7.32
7.31
7.30
7.11
7.09
7.06
7.05
7.05
7.03
6.76
6.74
6.73
6.68
6.67
5.10
4.89
3.73
3.71
3.70
3.35
3.34
3.32
3.31
3.28
3.27
3.25
2.05
2.03
2.02
2.01
1.99
1.98
1.80
1.79
1.78
1.76
1.75
1.73
^{1}H NMR (500 MHz, $CDCl_3$)
NHCbz
N
H
S2a′
4.18
1.26
1.02
1.15
1.08
1.01
1.99
0.83
1.15
2.13
2.12
1.33
1.48
f1 (ppm)

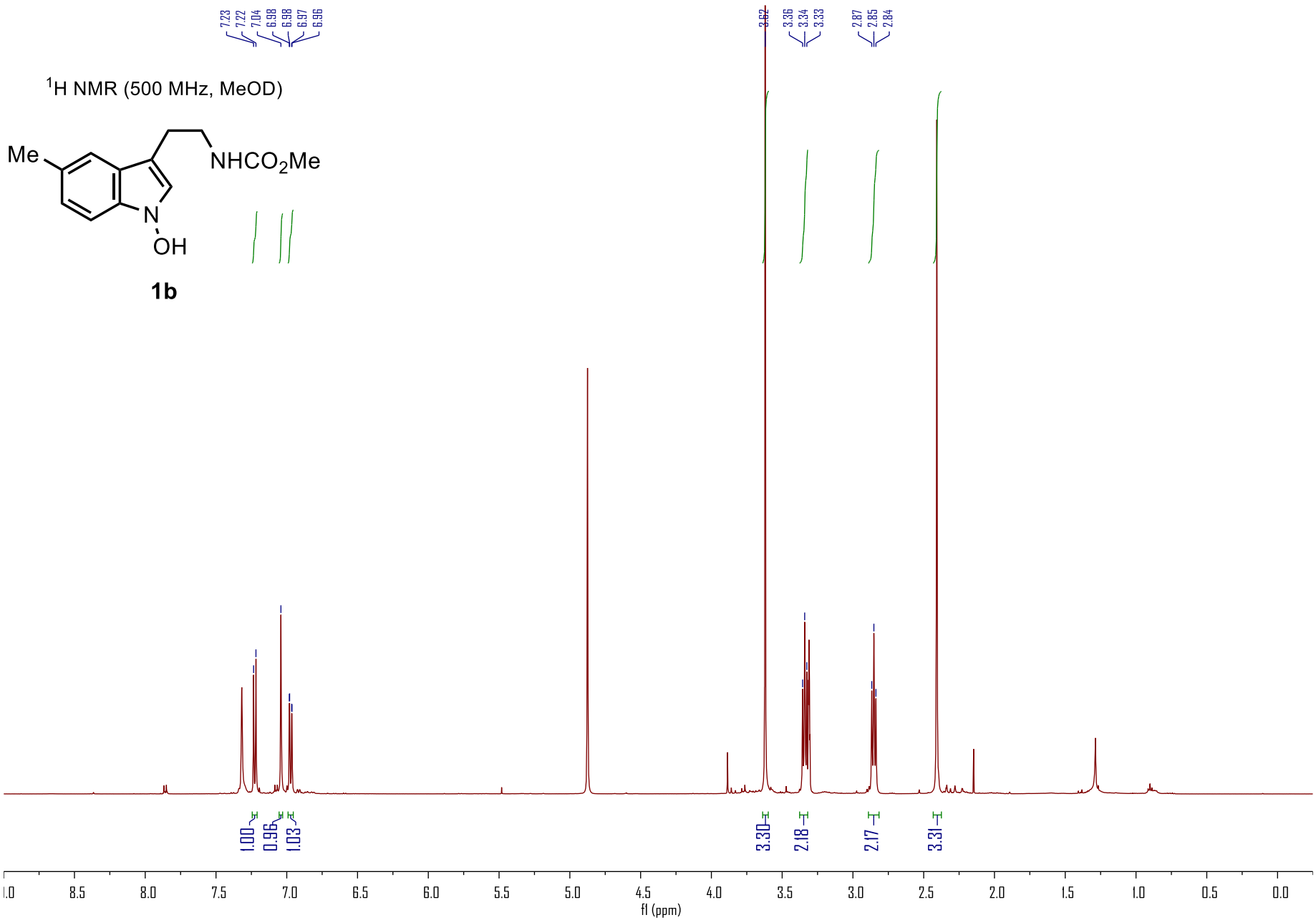

156.5
151.2
136.6
132.0
128.4
128.0
127.6
123.8
118.6
109.6
66.5
53.1
39.4
39.0
34.3
^{13}C NMR (126 MHz, $CDCl_3$)
NHCbz
N
H
S2a′
f1 (ppm)

^{1}H NMR (500 MHz, MeOD)

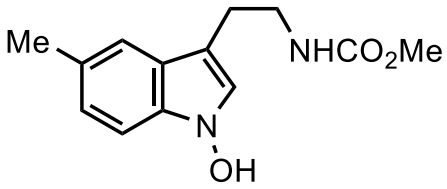


1a

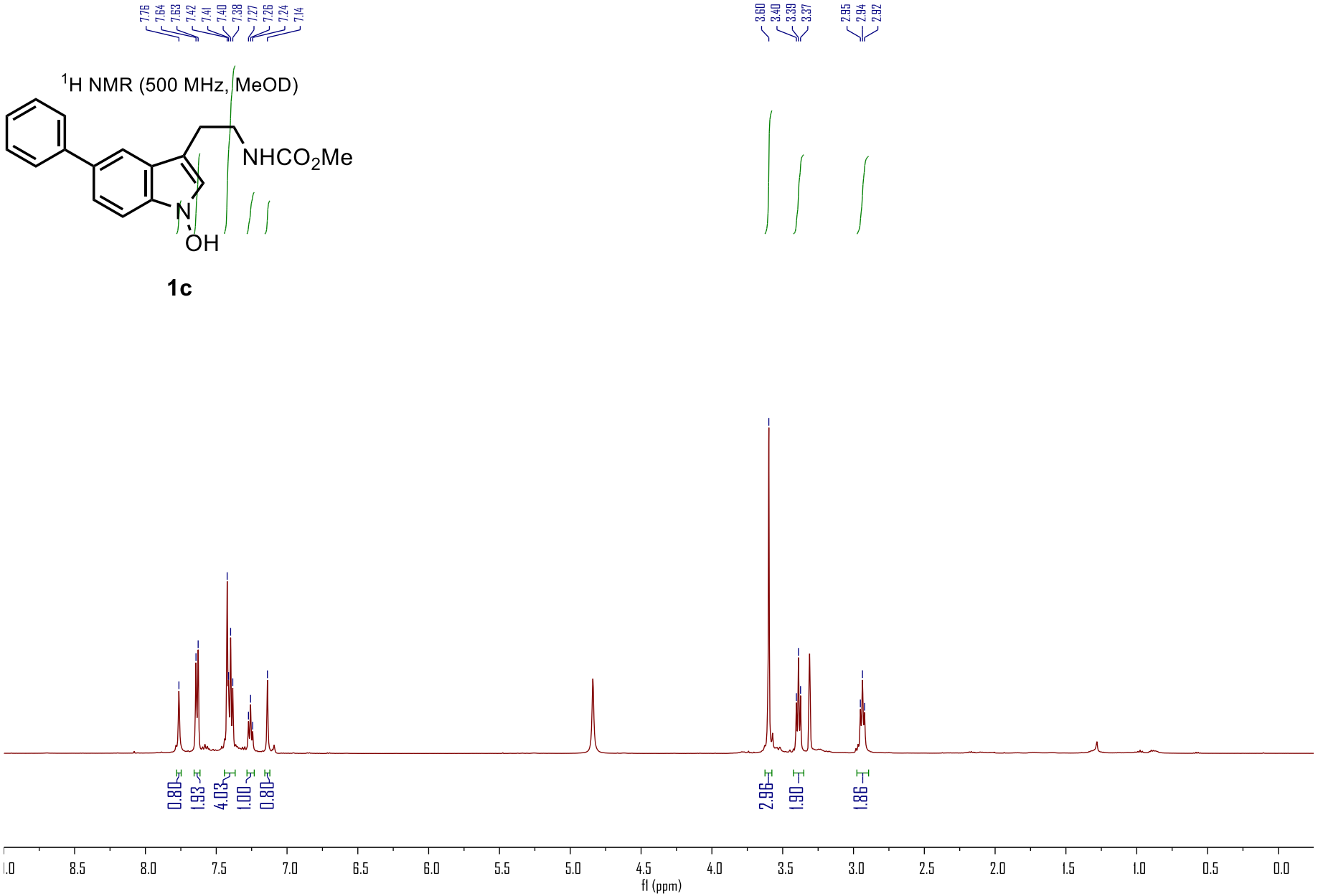

159.6
135.7
125.1
124.4
122.7
119.7
119.5
109.2
108.8
52.4
42.8
26.6
^{13}C NMR (126 MHz, MeOD)
NHCO$_2$Me
N
OH
1a
f1 (ppm)

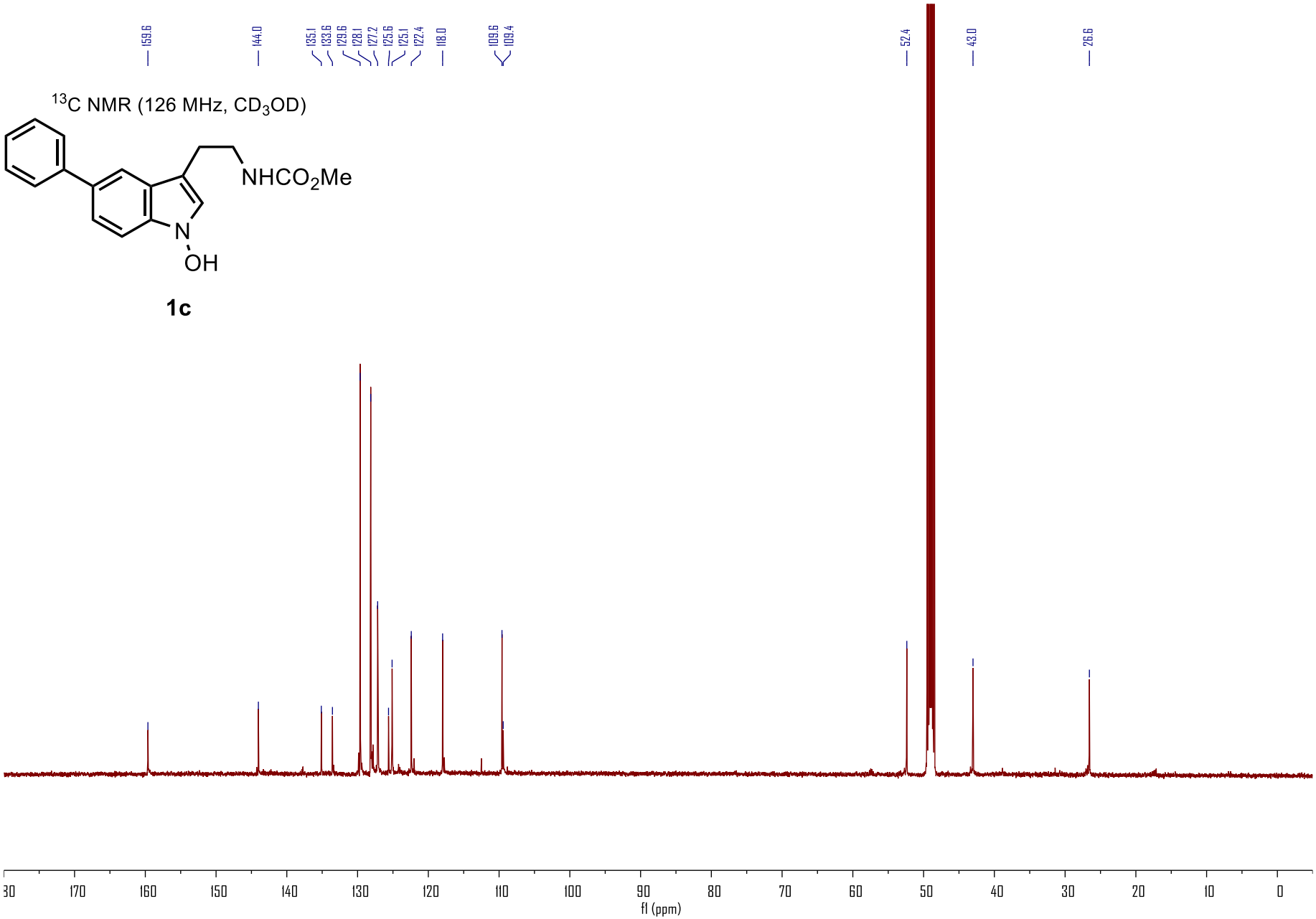

7.23
7.22
7.04
6.98
6.98
6.97
6.96
3.82
3.36
3.34
3.33
2.87
2.85
2.84
1H NMR (500 MHz, MeOD)
Me
NHCO2Me
N
OH
1b
1.00
0.96
1.03
3.30
2.18
2.17
3.31
f1 (ppm)

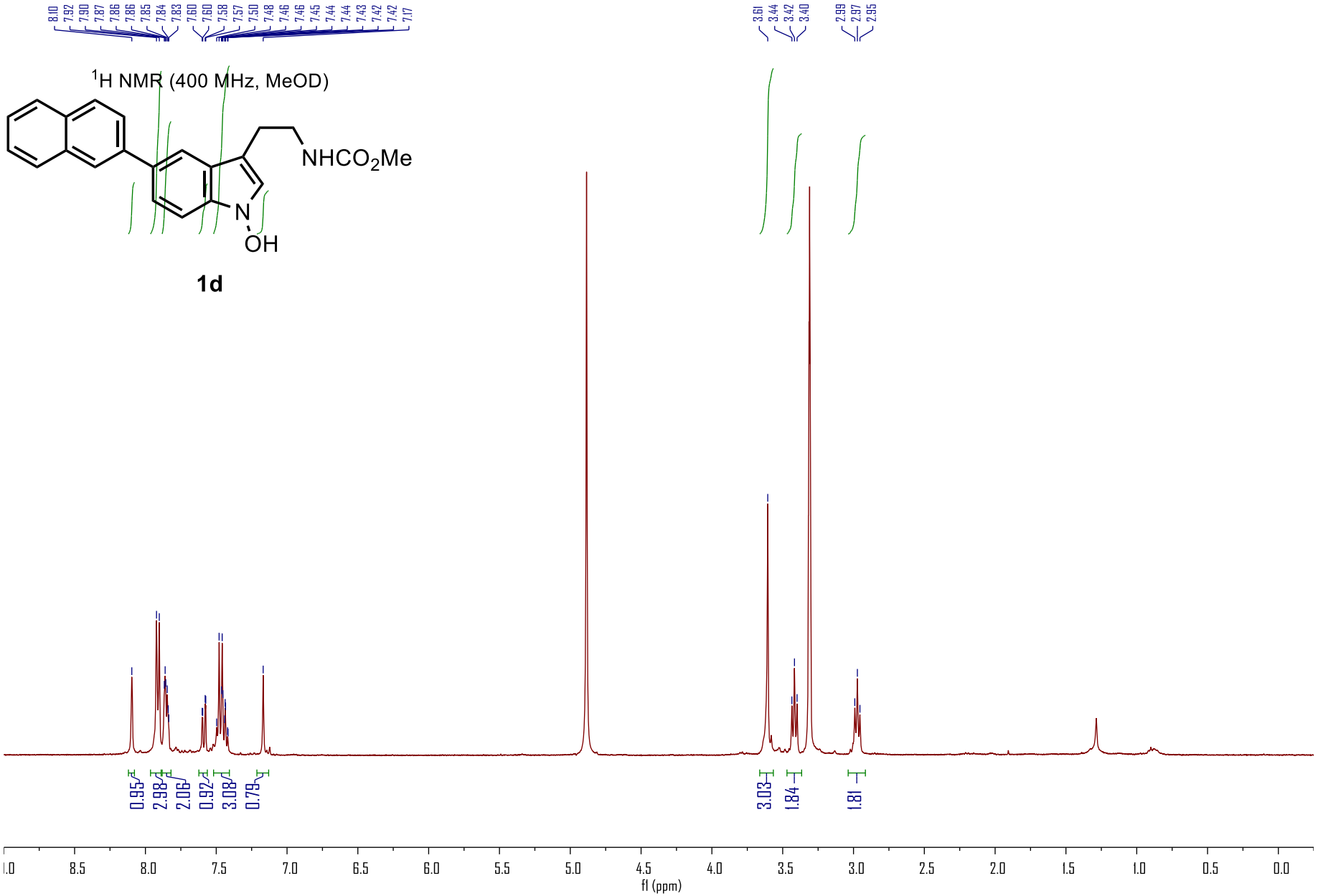
^{13}C NMR (126 MHz, MeOD)

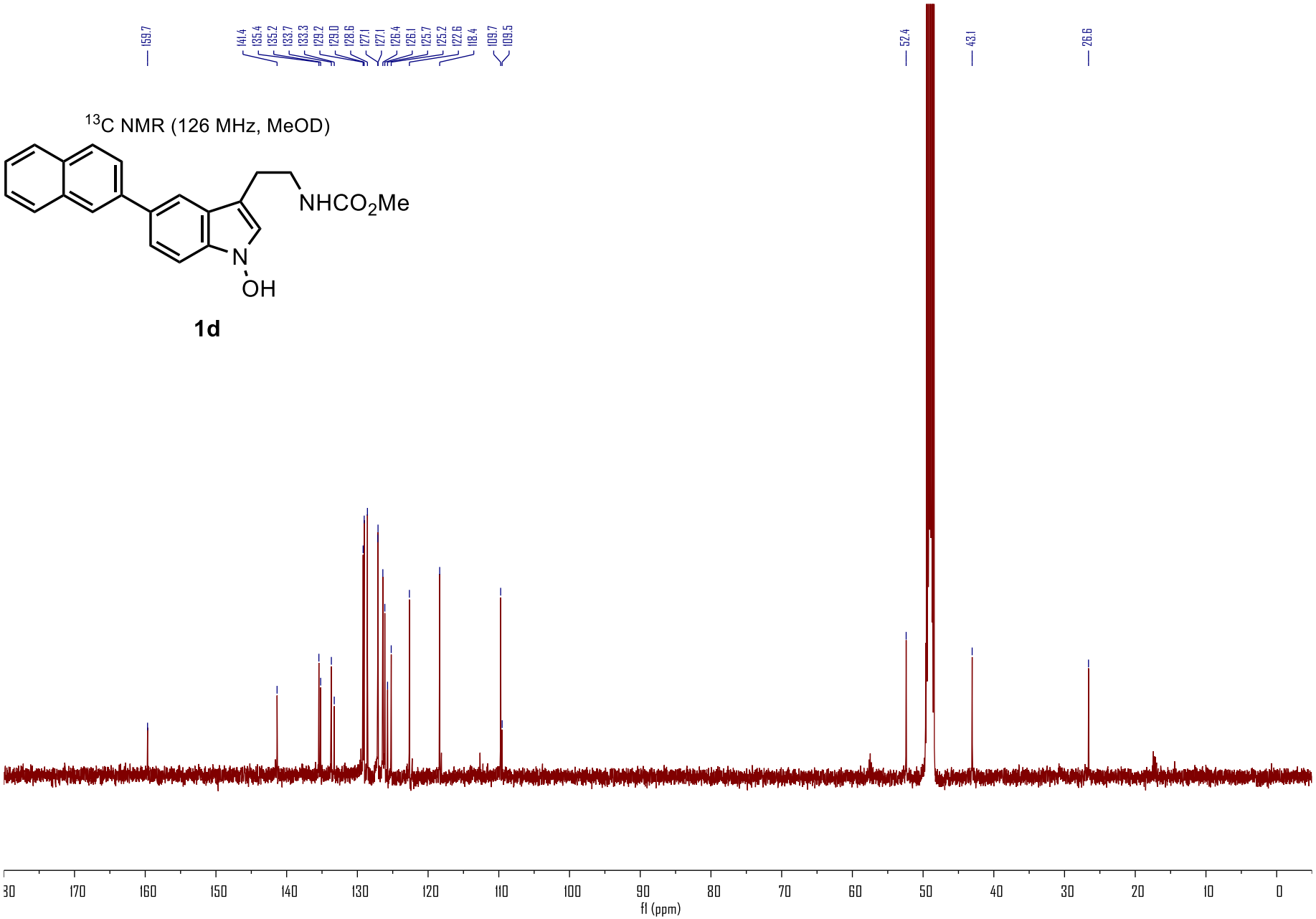


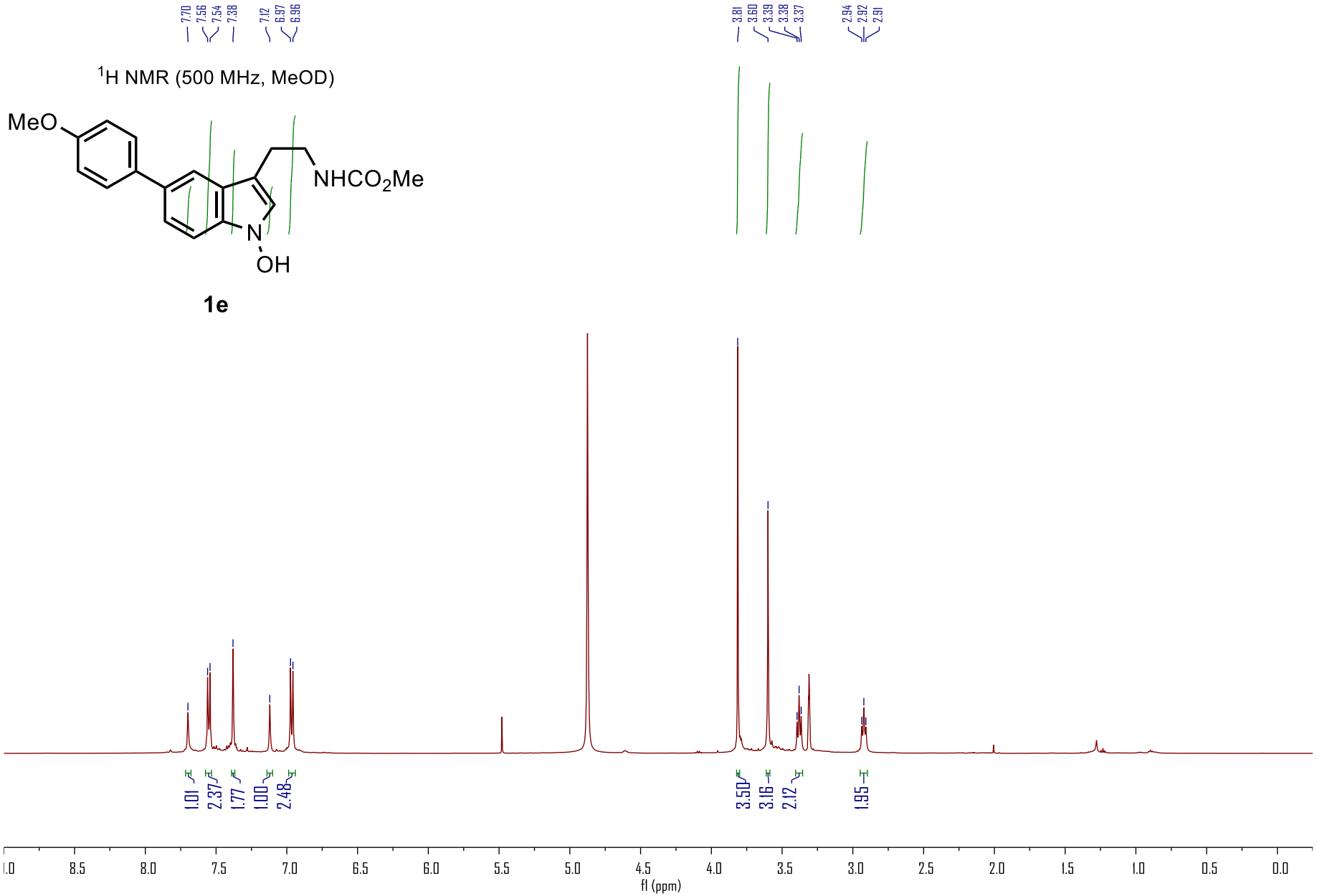
1b

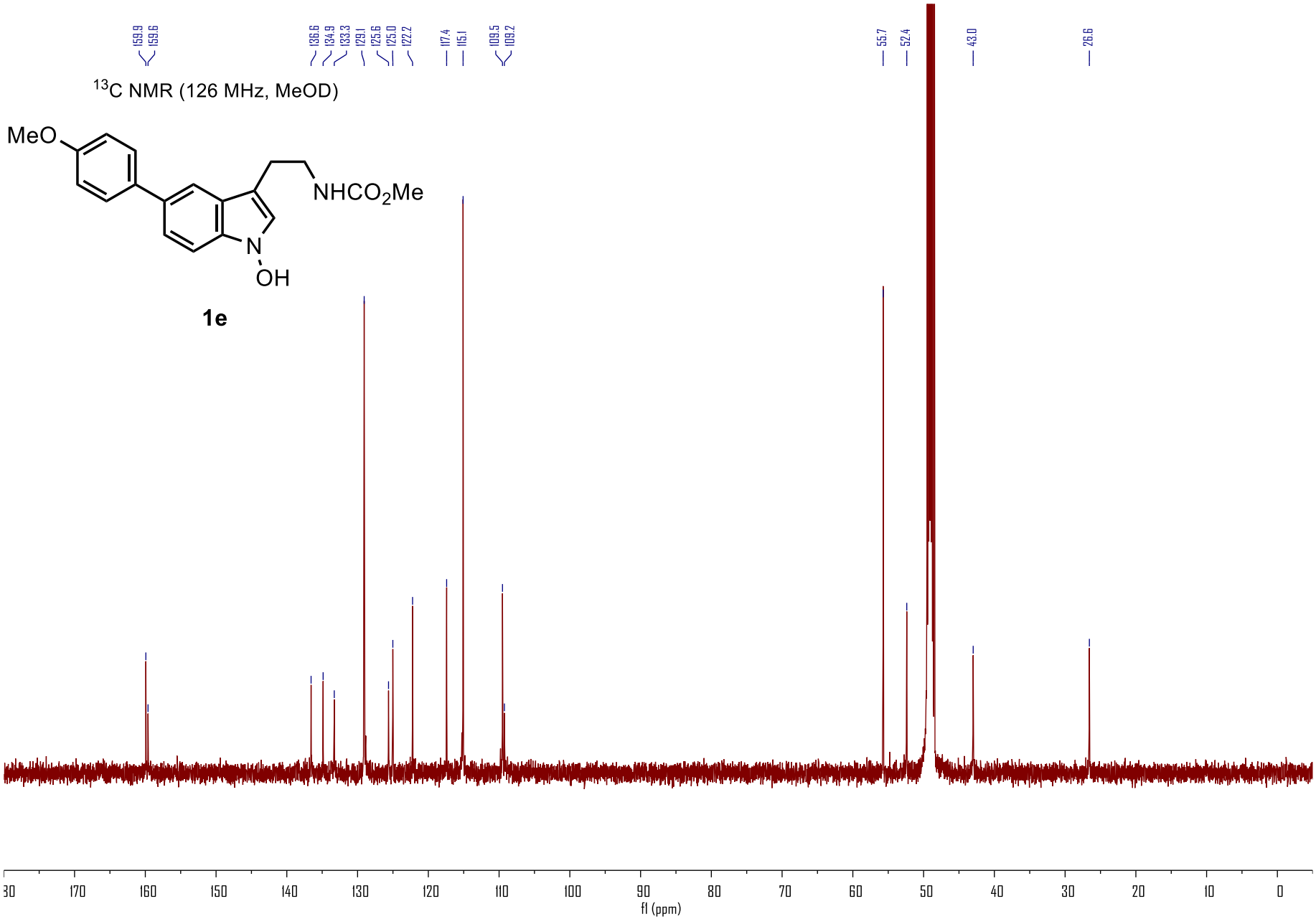

7.76
7.64
7.63
7.42
7.41
7.40
7.38
7.27
7.26
7.24
7.14
3.60
3.40
3.39
3.37
2.95
2.94
2.92
^{1}H NMR (500 MHz, MeOD)
NHCO$_2$Me
N
OH
1c
0.80
1.93
4.03
1.00
0.80
2.96
1.90
1.86
f1 (ppm)

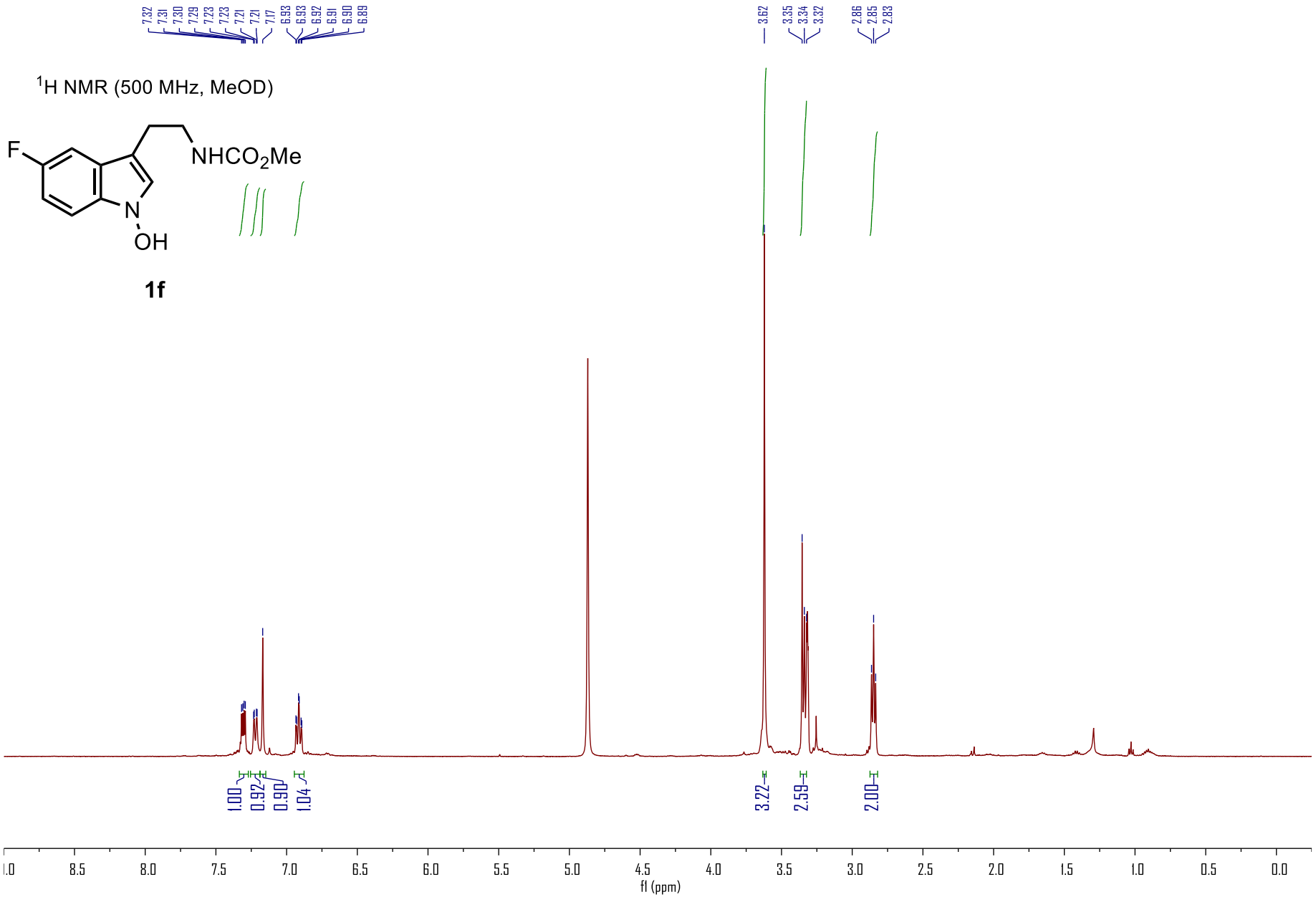

159.6
144.0
135.1
133.6
129.6
128.1
127.2
125.6
125.1
122.4
118.0
109.6
109.4
52.4
43.0
26.6
^{13}C NMR (126 MHz, CD_3OD)
$NHCO_2Me$
N
OH
1c
f1 (ppm)

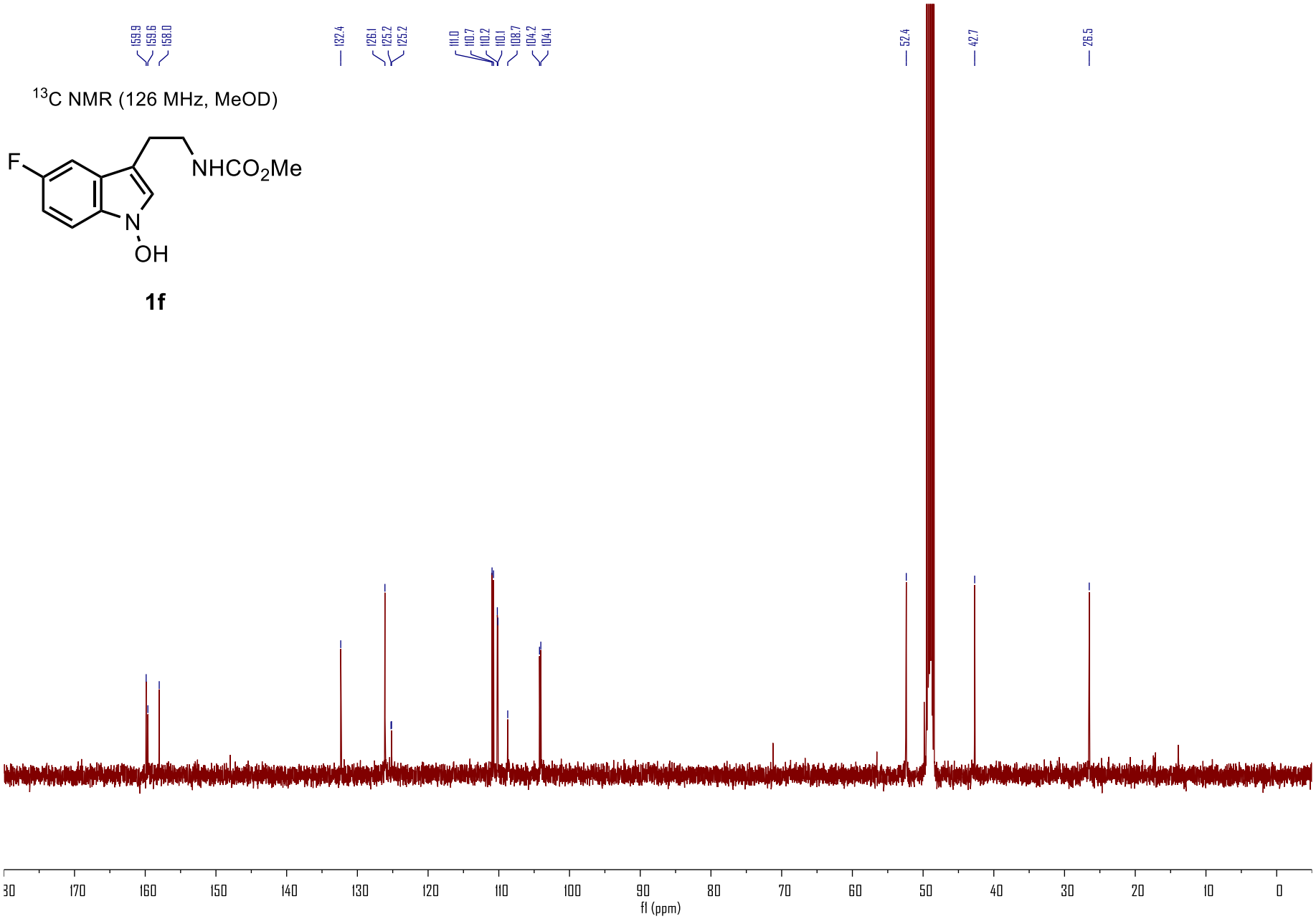

8.10
7.92
7.90
7.87
7.86
7.86
7.85
7.84
7.83
7.60
7.60
7.58
7.57
7.50
7.48
7.46
7.46
7.45
7.44
7.44
7.43
7.42
7.42
7.17
3.61
3.44
3.42
3.40
2.99
2.97
2.95
^{1}H NMR (400 MHz, MeOD)
NHCO$_2$Me
N
OH
1d
0.95
2.98
2.08
0.92
3.08
0.79
3.03
1.84
1.81
f1 (ppm)


159.7
141.4
135.4
135.2
133.7
133.3
129.2
129.0
128.6
127.1
127.1
126.4
126.1
125.7
125.2
122.6
118.4
109.7
109.5
52.4
43.1
26.6
^{13}C NMR (126 MHz, MeOD)
NHCO$_2$Me
N
OH
1d
f1 (ppm)

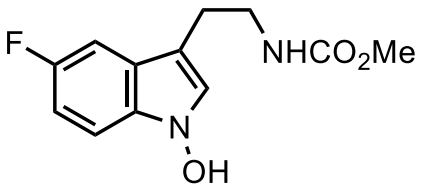

7.70
7.56
7.54
7.38
7.12
6.97
6.96
3.81
3.60
3.39
3.38
3.37
2.94
2.92
2.91
^{1}H NMR (500 MHz, MeOD)
MeO
NHCO$_2$Me
N
OH
1e
1.01
2.37
1.77
1.00
2.48
3.50
3.16
2.12
1.95
f1 (ppm)


159.9
159.6
136.8
134.9
133.3
129.1
125.6
125.0
122.2
117.4
115.1
109.5
109.2
55.7
52.4
43.0
26.6
^{13}C NMR (126 MHz, MeOD)
MeO
NHCO$_2$Me
N
OH
1e
f1 (ppm)

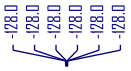

7.32
7.31
7.30
7.29
7.23
7.23
7.21
7.21
7.17
6.93
6.93
6.92
6.91
6.90
6.89
3.62
3.35
3.34
3.32
2.86
2.85
2.83
1H NMR (500 MHz, MeOD)
F
NHCO2Me
N
OH
1f
1.00
0.92
0.90
1.04
3.22
2.59
2.00
f1 (ppm)

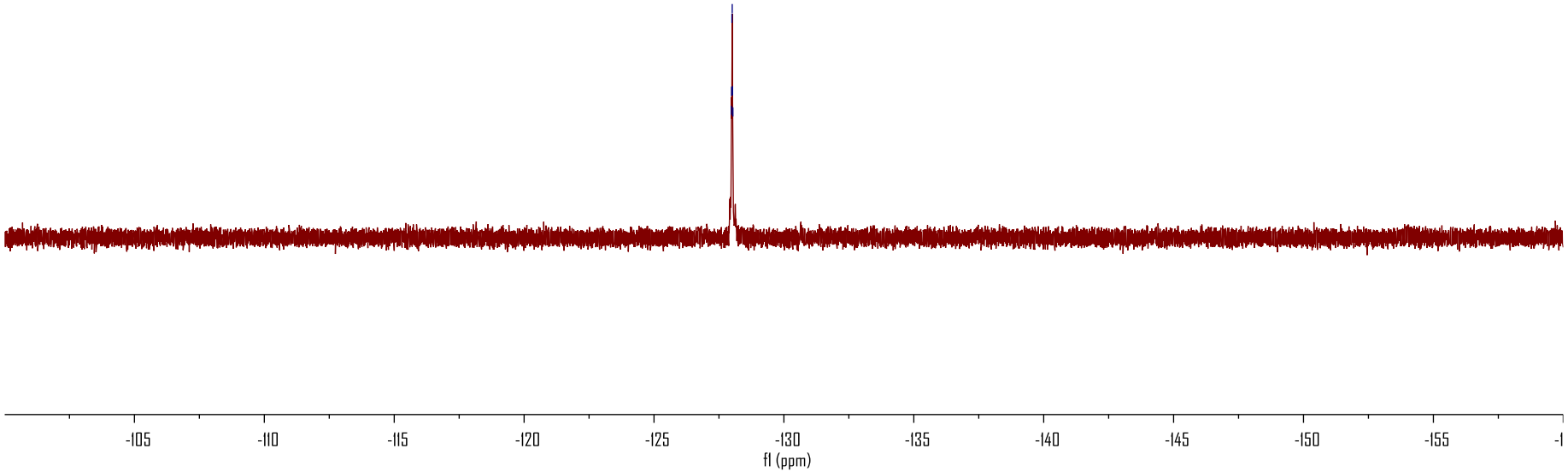

159.9
159.6
158.0
132.4
126.1
125.2
125.2
111.0
110.7
110.2
110.1
108.7
104.2
104.1
52.4
42.7
26.5
13C NMR (126 MHz, MeOD)
F
NHCO2Me
N
OH
1f
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

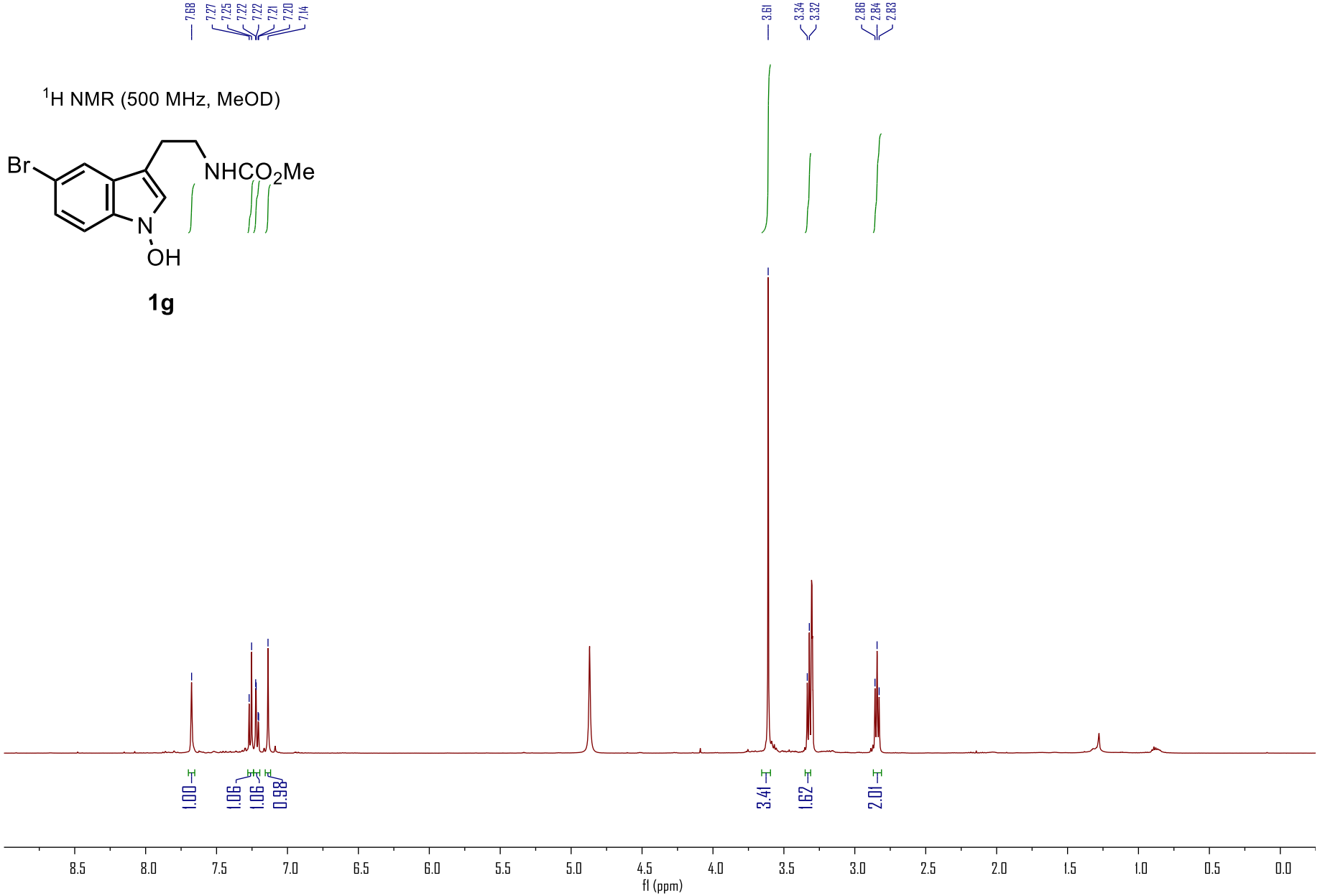
^{19}F NMR (376 MHz, MeOD)

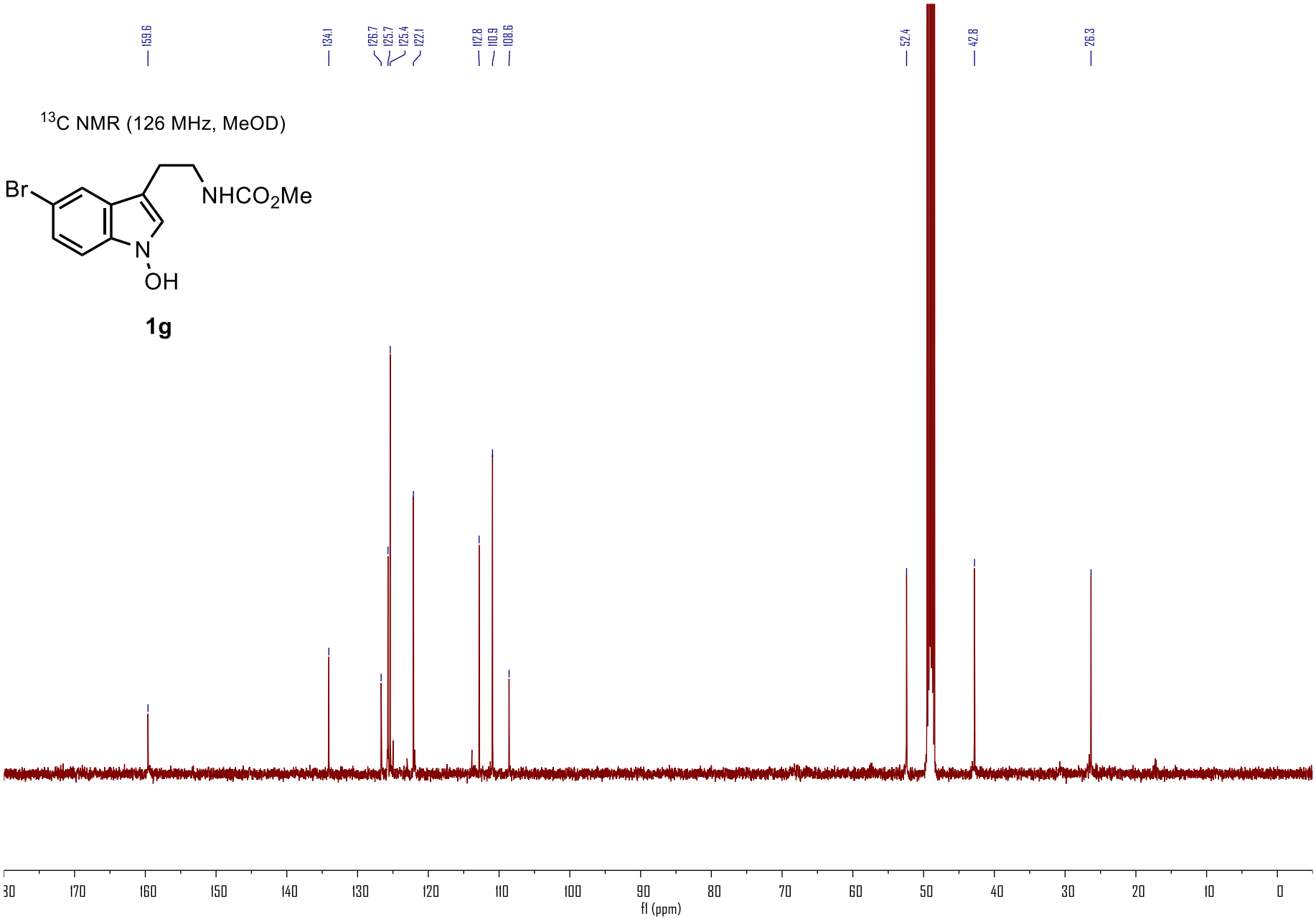


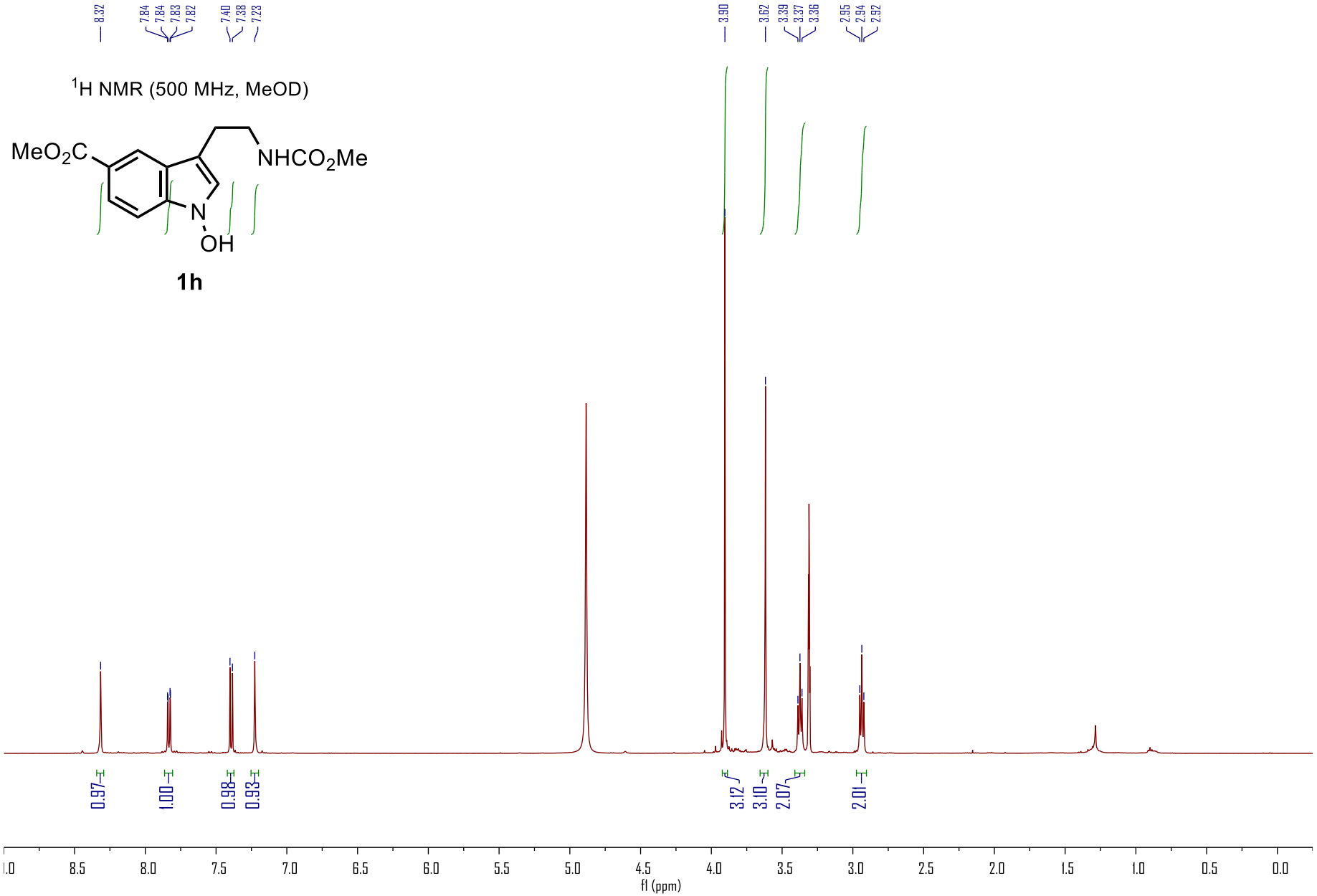
1f

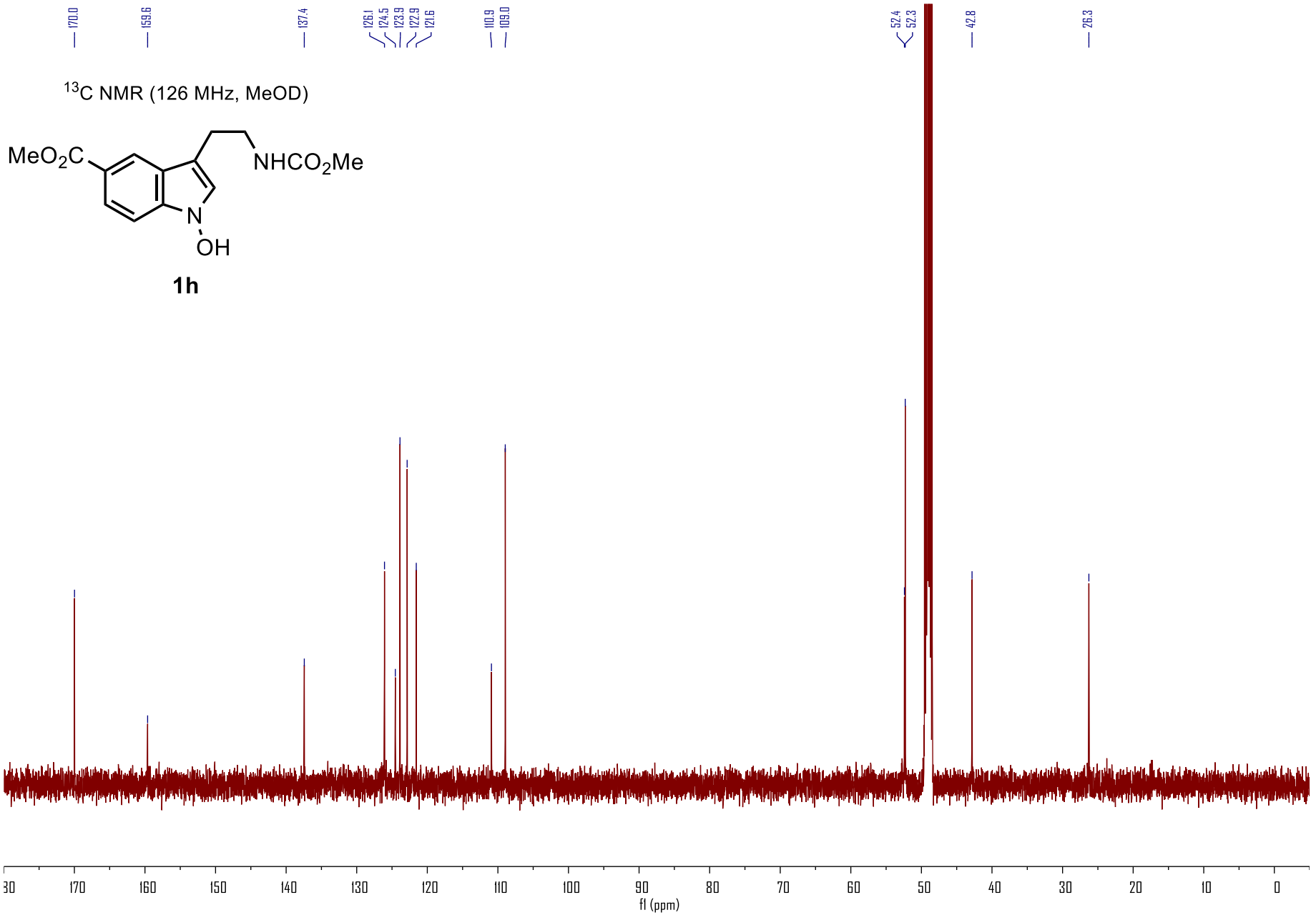


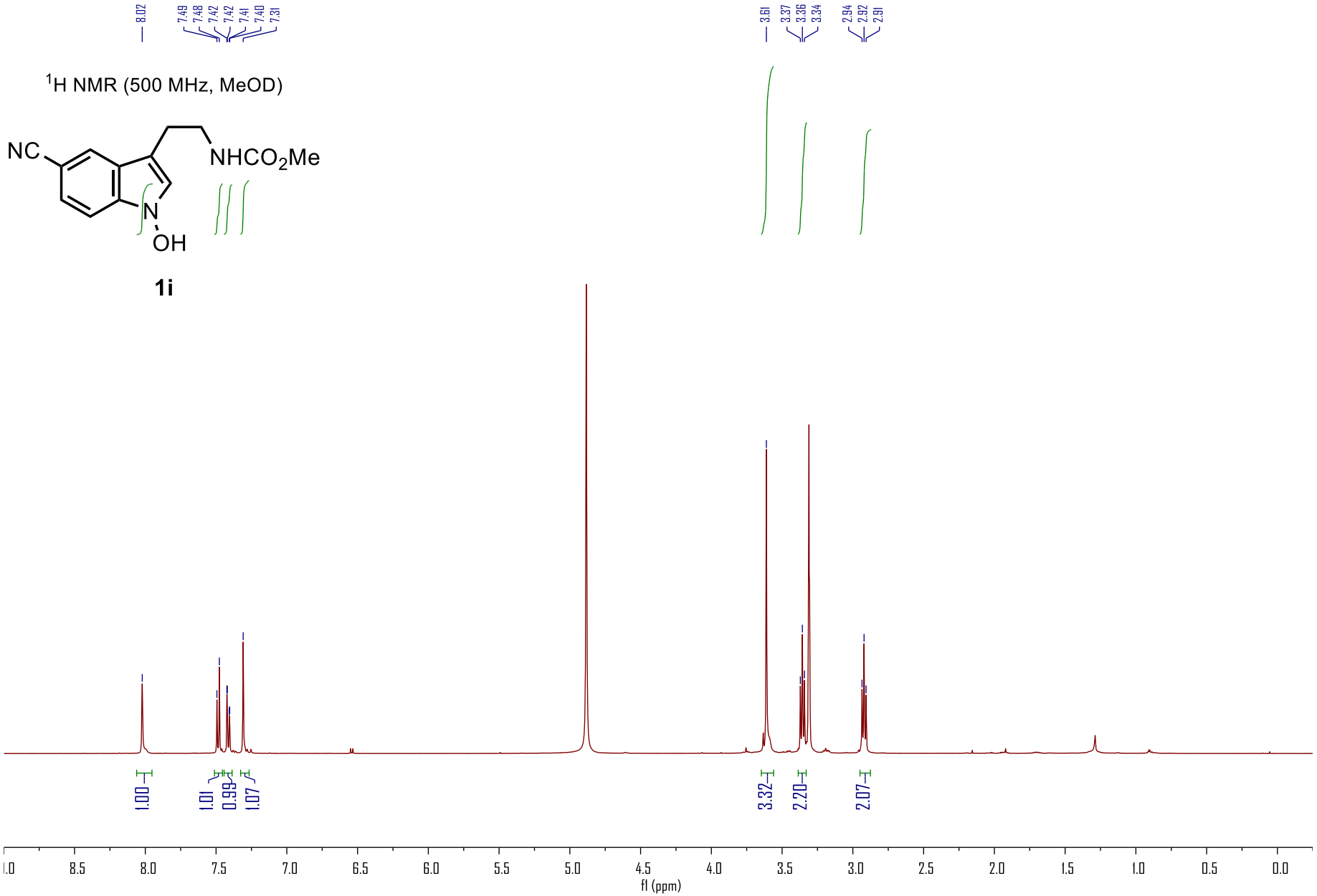


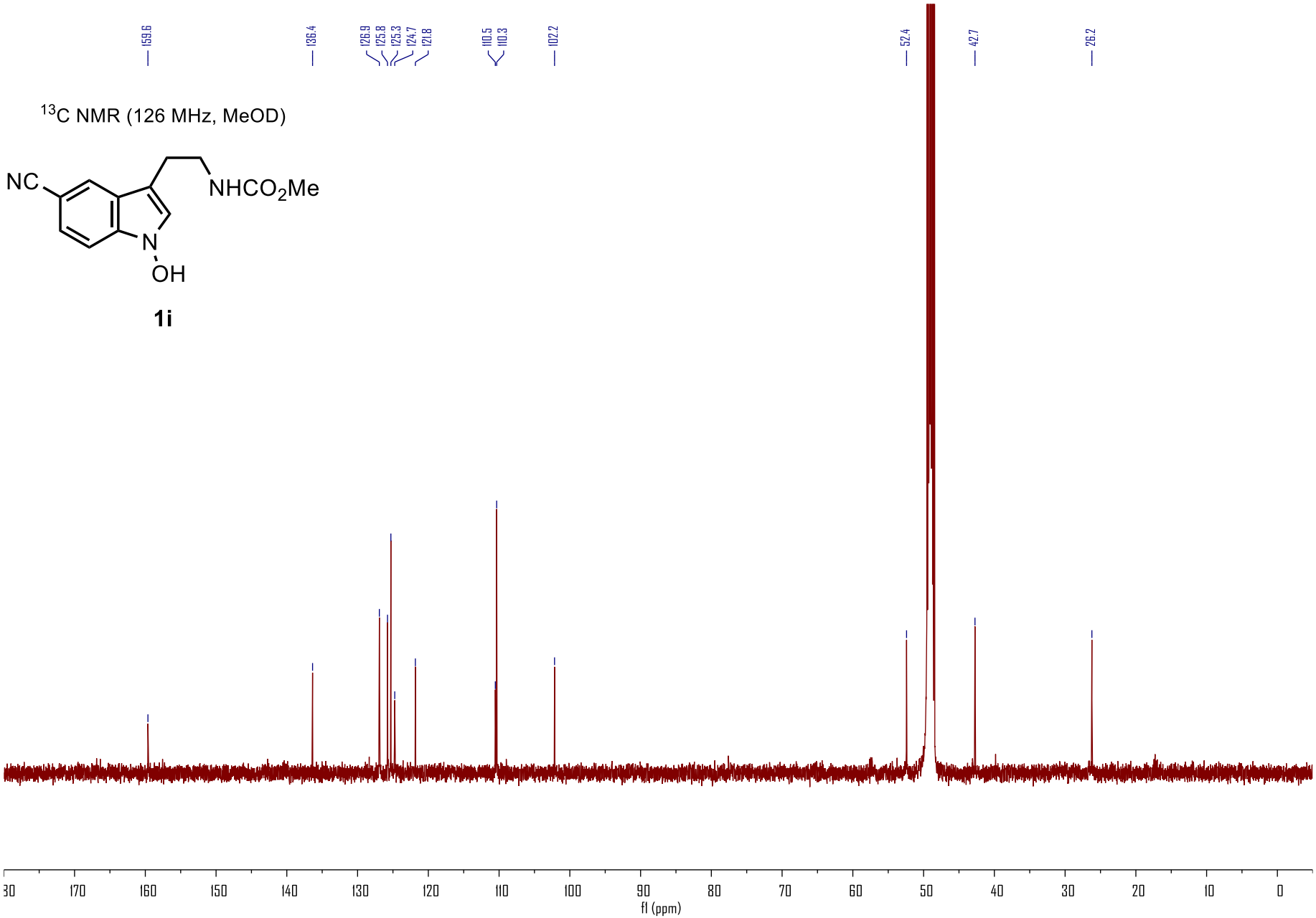

7.68
7.27
7.25
7.22
7.22
7.21
7.20
7.14
3.61
3.34
3.32
2.86
2.84
2.83
^{1}H NMR (500 MHz, MeOD)
Br
NHCO$_2$Me
N
OH
1g
1.00
1.06
1.06
0.98
3.41
1.62
2.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

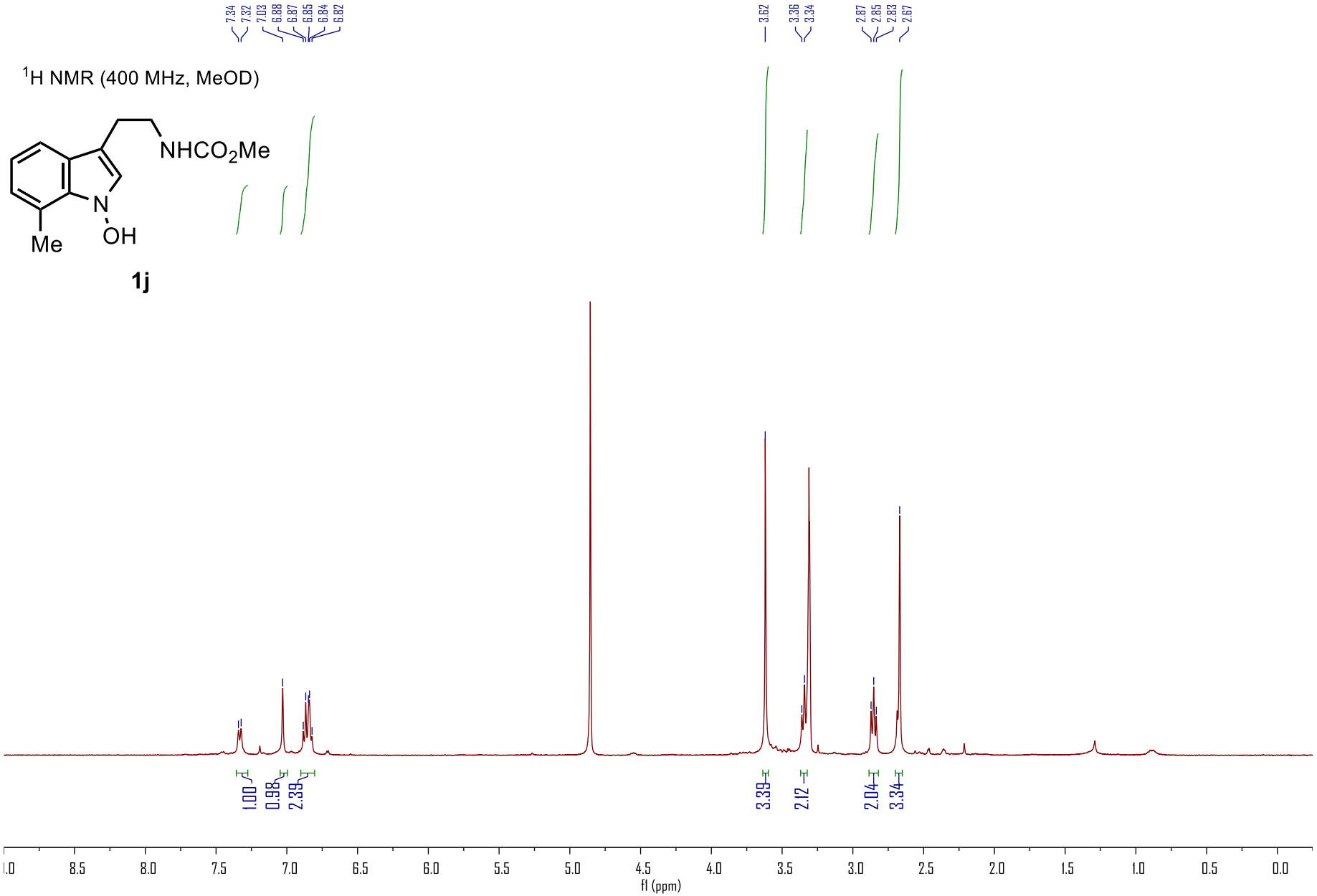

159.6
134.1
126.7
125.7
125.4
122.1
112.8
110.9
108.6
52.4
42.8
26.3
^{13}C NMR (126 MHz, MeOD)
Br
NHCO$_2$Me
N
OH
1g
f1 (ppm)


8.32
7.84
7.84
7.83
7.82
7.40
7.38
7.23
3.90
3.62
3.39
3.37
3.36
2.95
2.94
2.92
^{1}H NMR (500 MHz, MeOD)
MeO_2C
$NHCO_2Me$
N
OH
1h
0.97
1.00
0.98
0.93
3.12
3.10
2.07
2.01
f1 (ppm)

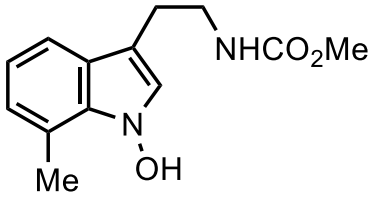

170.0
159.6
137.4
126.1
124.5
123.9
122.9
121.6
110.9
109.0
52.4
52.3
42.8
26.3
^{13}C NMR (126 MHz, MeOD)
MeO$_2$C
NHCO$_2$Me
N
OH
1h
f1 (ppm)


8.02
7.49
7.48
7.42
7.42
7.41
7.40
7.31
3.61
3.37
3.36
3.34
2.94
2.92
2.91
^{1}H NMR (500 MHz, MeOD)
NC
NHCO$_2$Me
N
OH
1i
1.00
1.01
0.99
1.07
3.32
2.20
2.07
f1 (ppm)

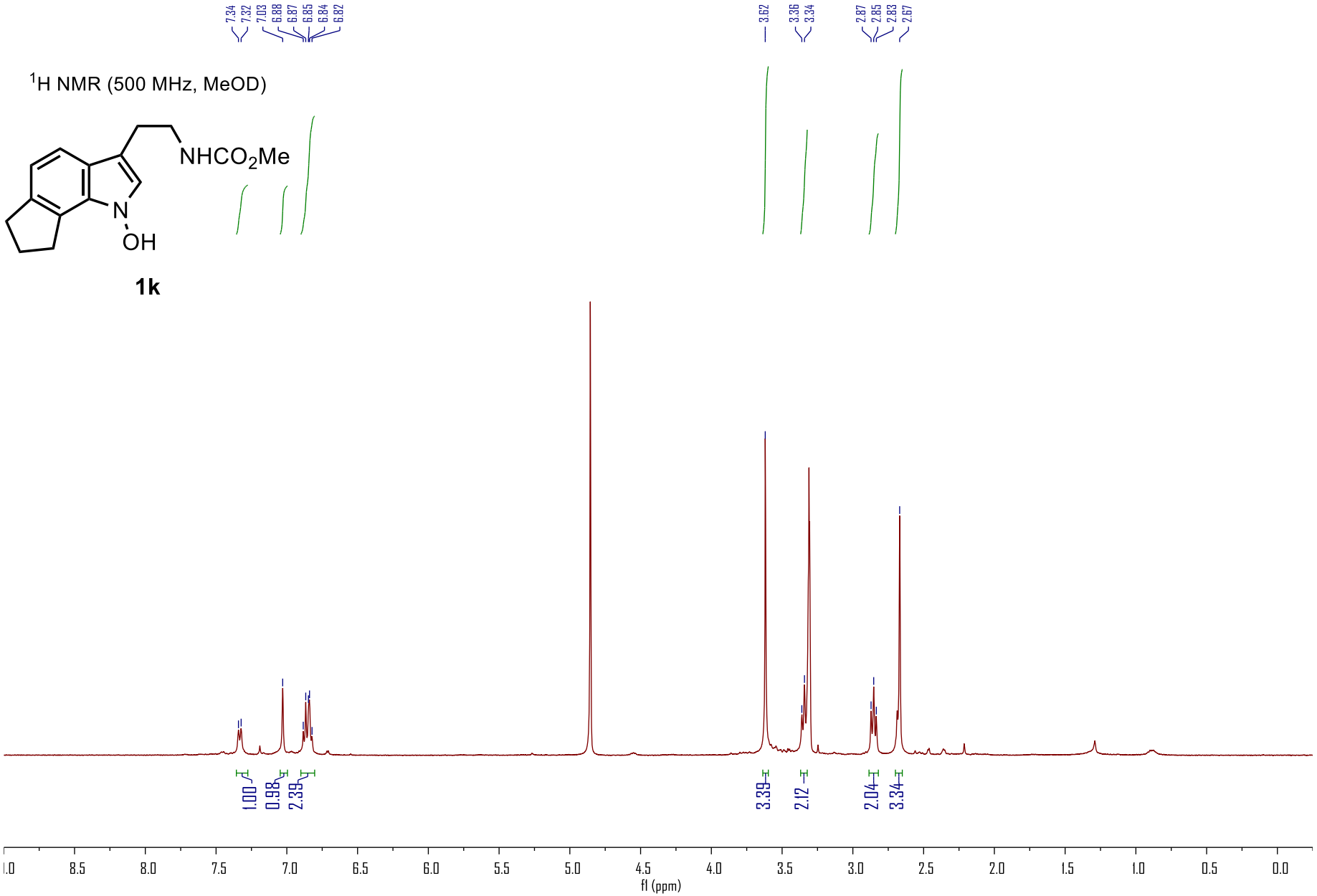

159.6
136.4
126.9
125.8
125.3
124.7
121.8
110.5
110.3
102.2
52.4
42.7
26.2
^{13}C NMR (126 MHz, MeOD)
NC
NHCO$_2$Me
N
OH
1i
f1 (ppm)


7.34
7.32
7.03
6.88
6.87
6.85
6.84
6.82
3.62
3.36
3.34
2.87
2.85
2.83
2.67
^{1}H NMR (400 MHz, MeOD)
NHCO$_2$Me
N
OH
Me
1j
1.00
0.98
2.39
3.39
2.12
2.04
3.34
f1 (ppm)

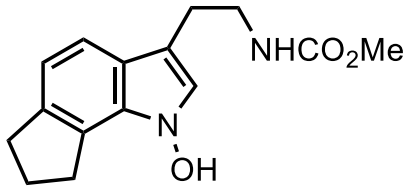
^{13}C NMR (101 MHz, MeOD)



1j

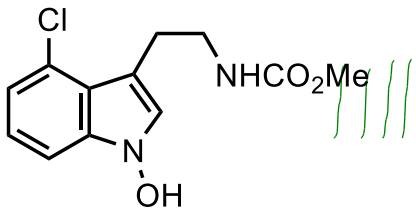

7.34
7.32
7.03
6.88
6.87
6.85
6.84
6.82
3.62
3.36
3.34
2.87
2.85
2.83
2.67
^{1}H NMR (500 MHz, MeOD)
NHCO$_2$Me
N
OH
1k
1.00
0.98
2.39
3.39
2.12
2.04
3.34
f1 (ppm)

^{13}C NMR (126 MHz, MeOD)

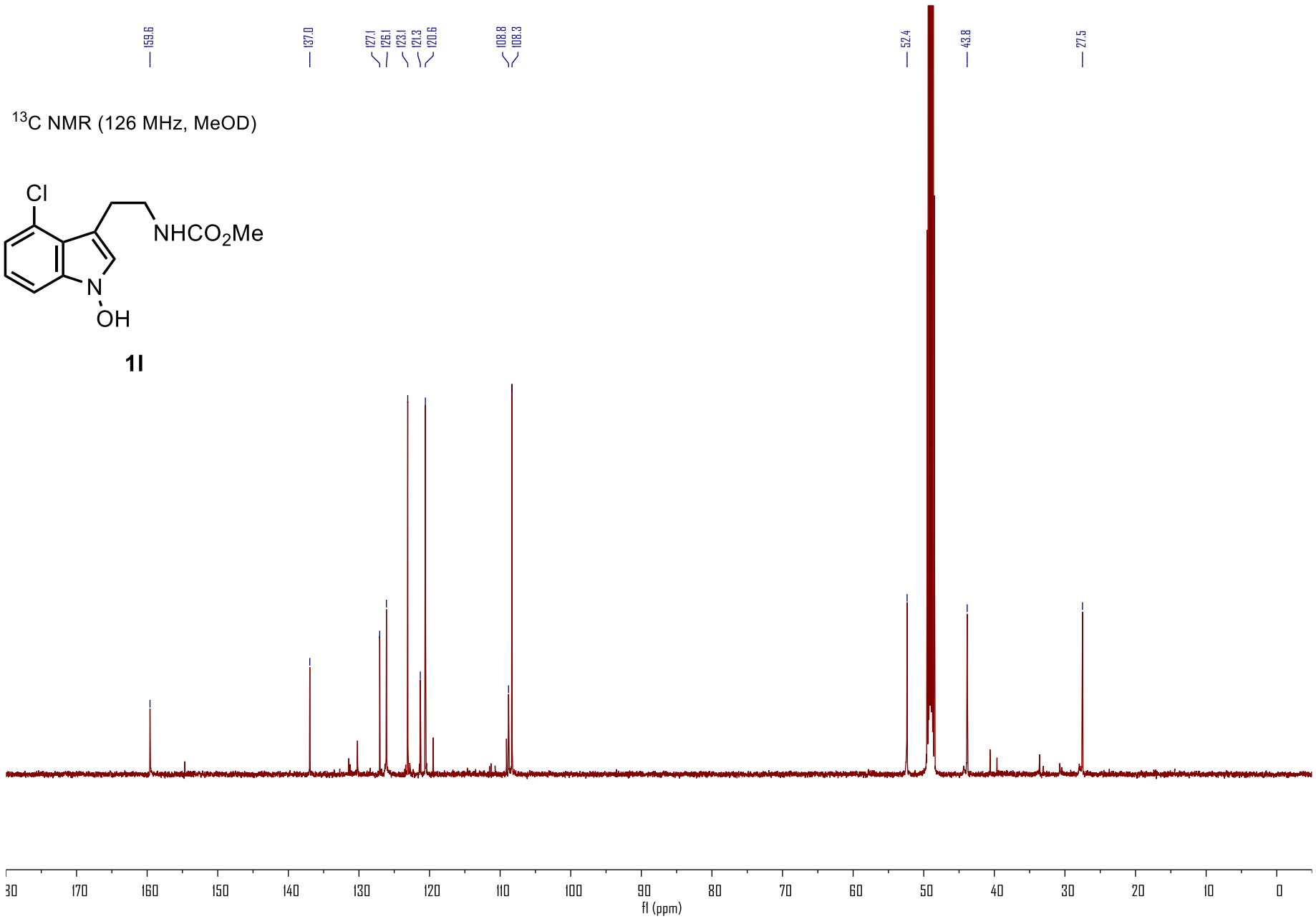


1k

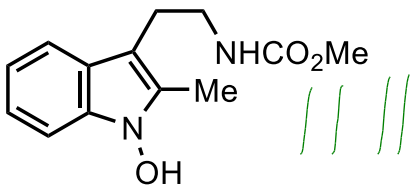
^{1}H NMR (500 MHz, MeOD)



1l

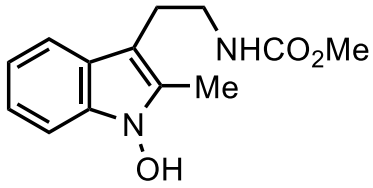

159.6
137.0
127.1
126.1
123.1
121.3
120.6
108.8
108.3
52.4
43.8
27.5
^{13}C NMR (126 MHz, MeOD)
Cl
NHCO$_2$Me
N
OH
1l
f1 (ppm)

^{1}H NMR (500 MHz, MeOD)

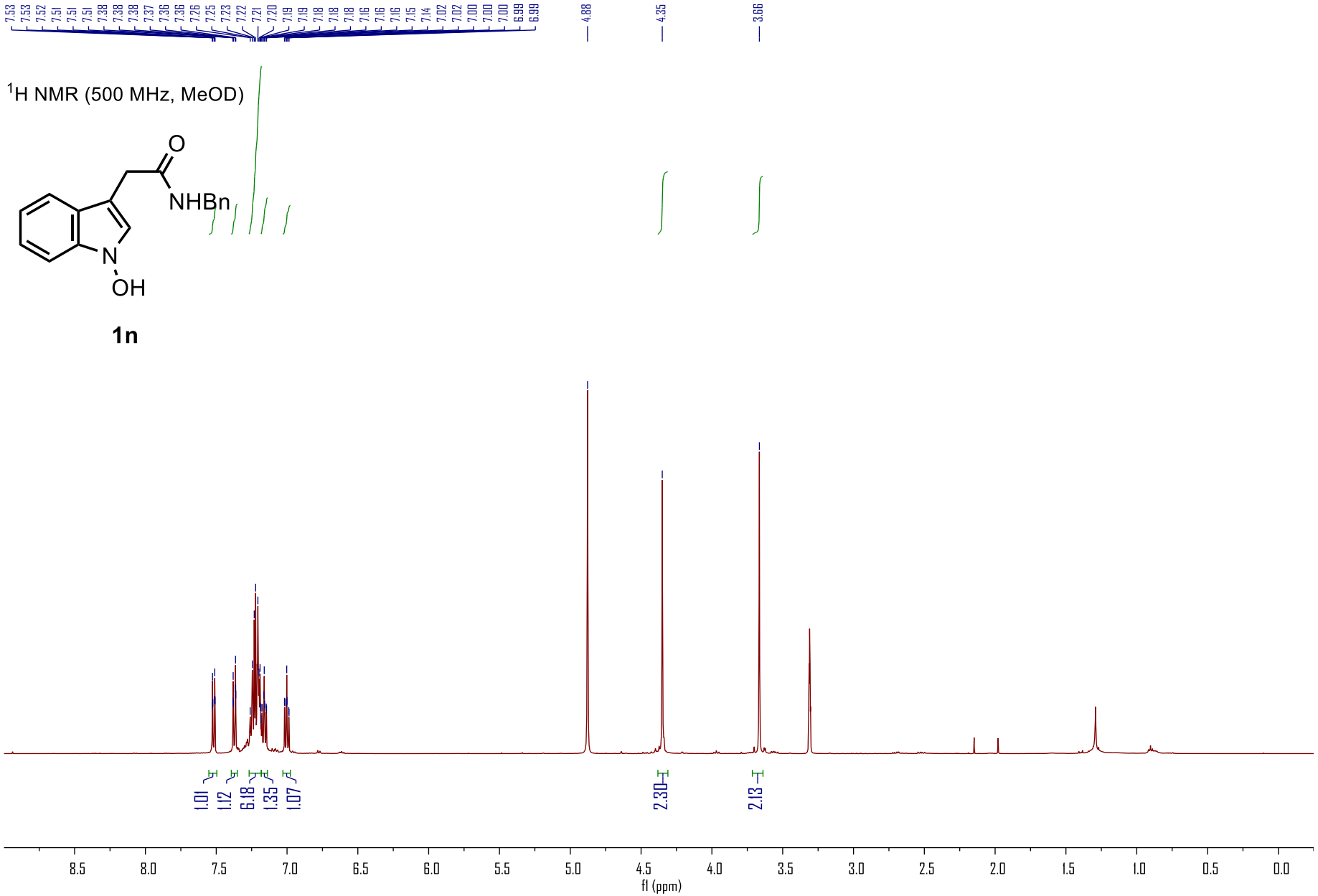


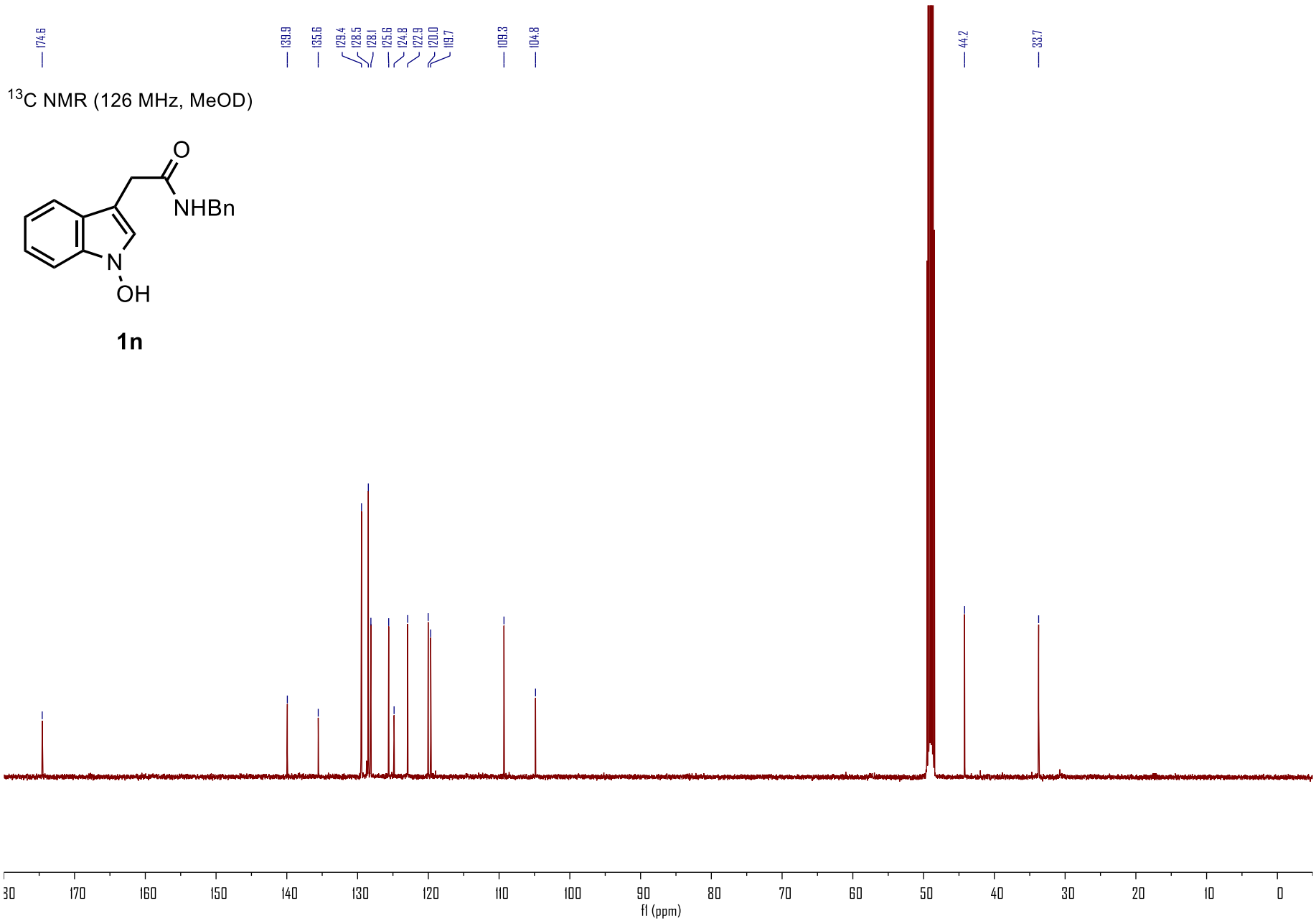
1m

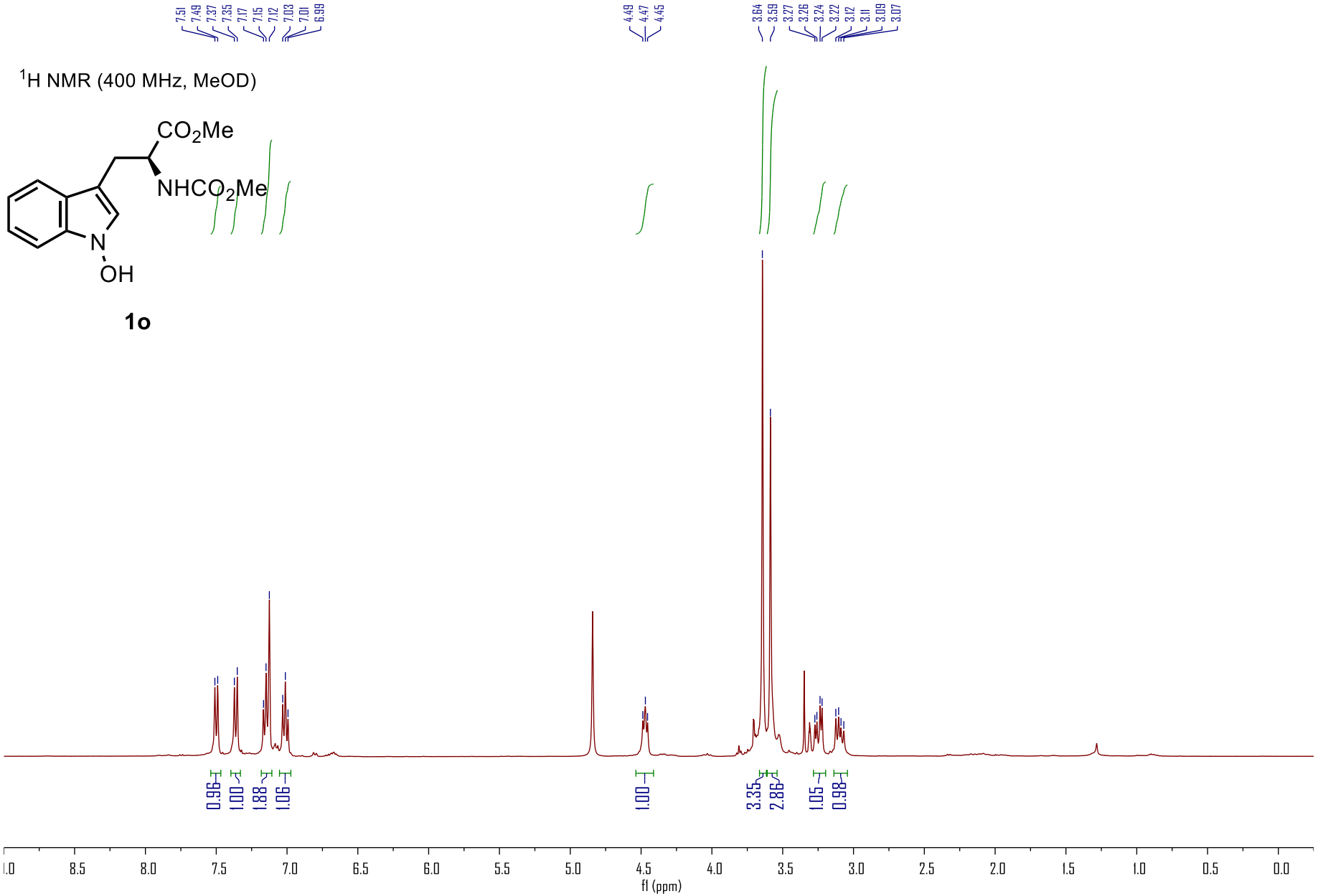
^{13}C NMR (126 MHz, MeOD)

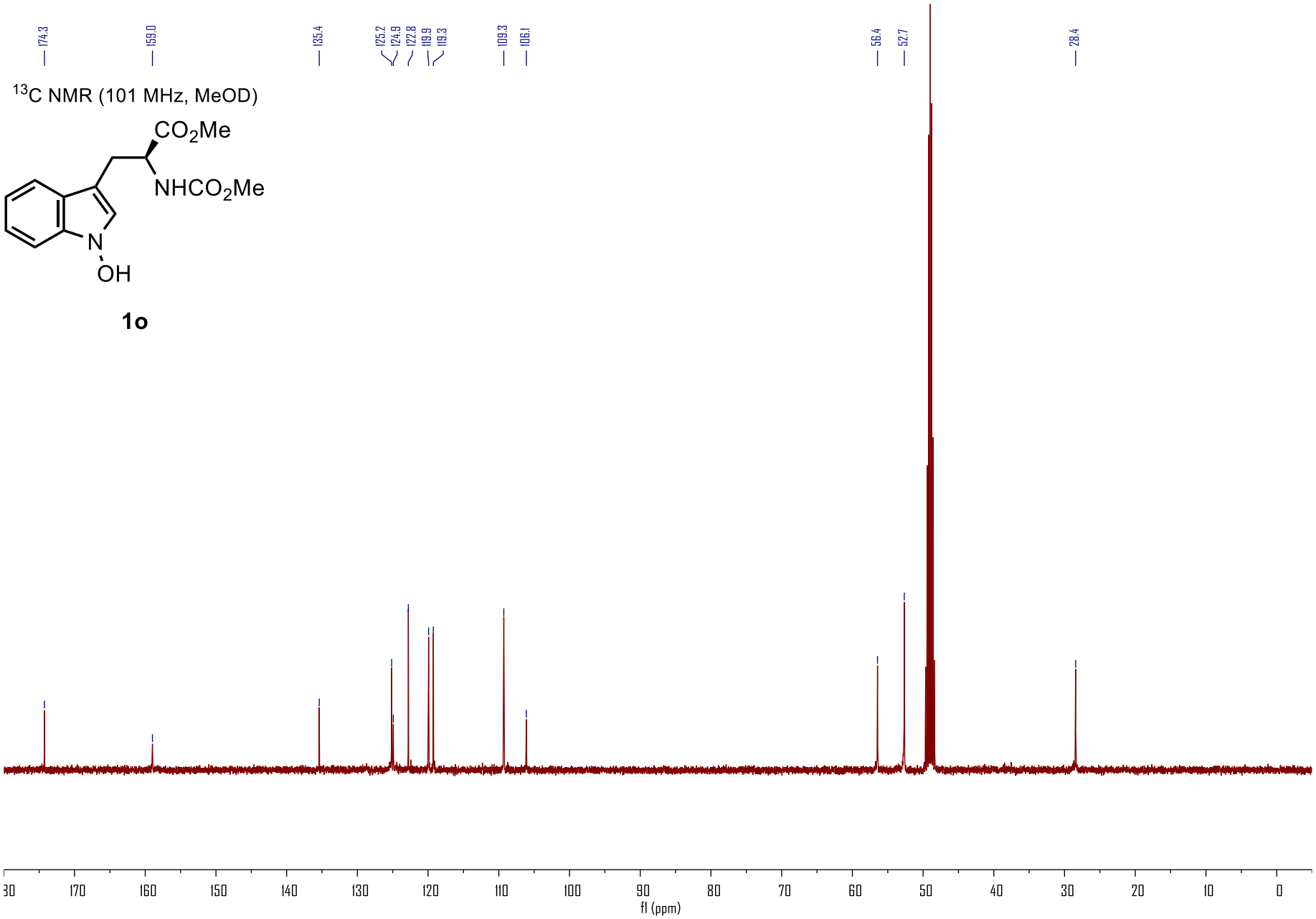


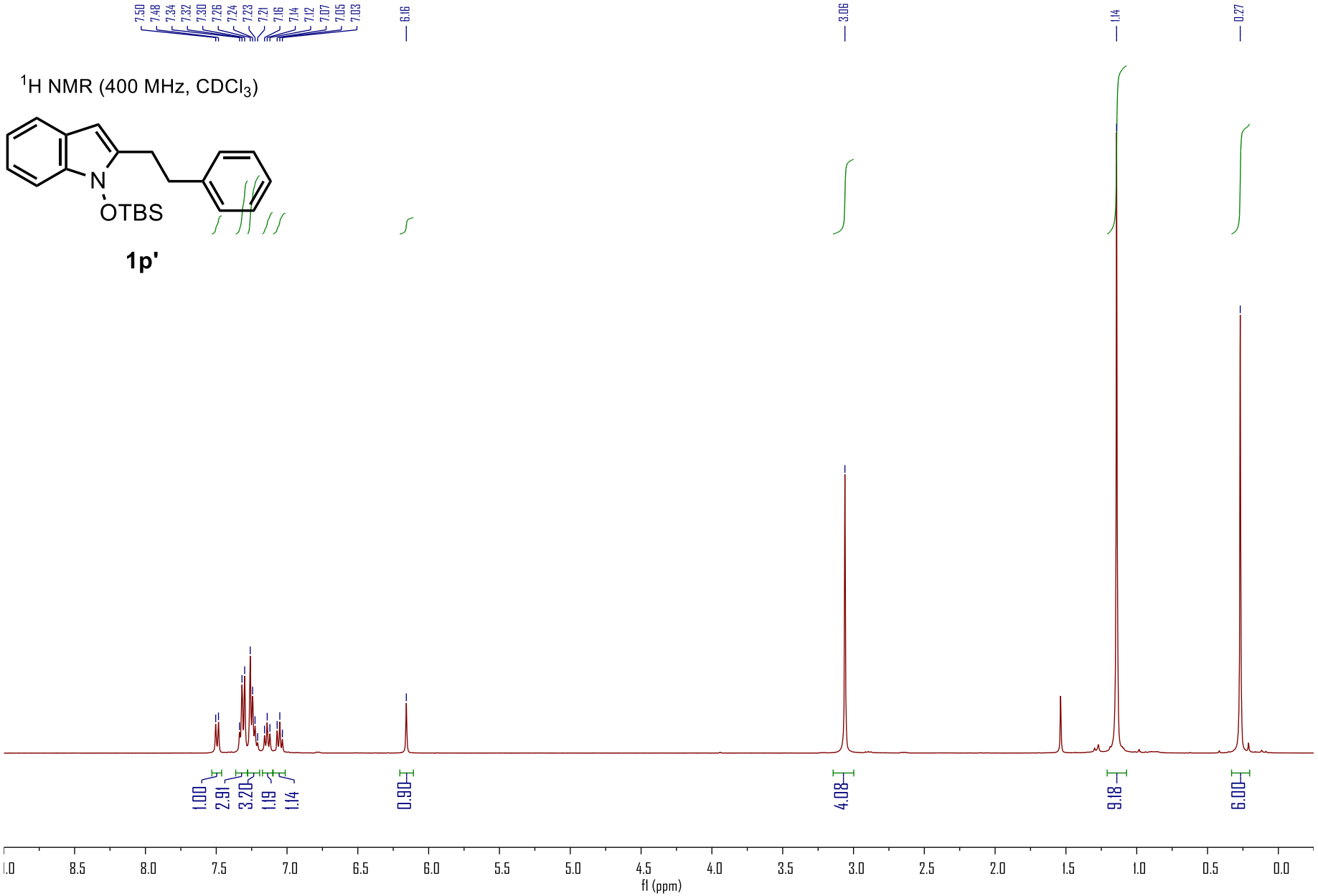
1m


7.53
7.53
7.52
7.51
7.51
7.51
7.38
7.38
7.38
7.37
7.36
7.36
7.26
7.25
7.23
7.22
7.21
7.20
7.19
7.19
7.18
7.18
7.18
7.16
7.16
7.16
7.15
7.14
7.02
7.02
7.00
7.00
7.00
6.99
6.99
4.88
4.35
3.66
1H NMR (500 MHz, MeOD)
O
NHBn
N
OH
1n
1.01
1.12
6.18
1.35
1.07
2.30
2.13
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

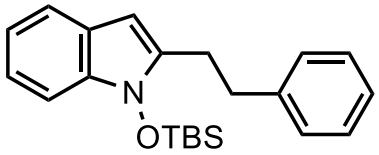

174.6
139.9
135.6
129.4
128.5
128.1
125.6
124.8
122.9
120.0
119.7
109.3
104.8
44.2
33.7
13C NMR (126 MHz, MeOD)
O
NHBn
N
OH
1n
f1 (ppm)


7.51
7.49
7.37
7.35
7.17
7.15
7.12
7.03
7.01
6.99
4.49
4.47
4.45
3.64
3.59
3.27
3.26
3.24
3.22
3.12
3.11
3.09
3.07
^{1}H NMR (400 MHz, MeOD)
CO_2Me
$NHCO_2Me$
N
OH
1o
0.96
1.00
1.88
1.06
1.00
3.35
2.86
1.05
0.98
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


174.3
159.0
135.4
125.2
124.9
122.8
119.9
119.3
109.3
106.1
56.4
52.7
28.4
^{13}C NMR (101 MHz, MeOD)
CO_2Me
$NHCO_2Me$
N
OH
1o
f1 (ppm)

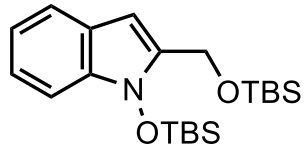

7.50
7.48
7.34
7.32
7.30
7.26
7.24
7.23
7.21
7.16
7.14
7.12
7.07
7.05
7.03
6.16
3.06
1.14
0.27
^{1}H NMR (400 MHz, $CDCl_3$)
N
OTBS
1p'
1.00
2.91
3.20
1.19
1.14
0.90
4.08
9.18
6.00
f1 (ppm)

^{13}C NMR (126 MHz, $CDCl_3$)



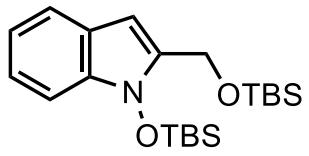
1p'

^{1}H NMR (400 MHz, $CDCl_3$)



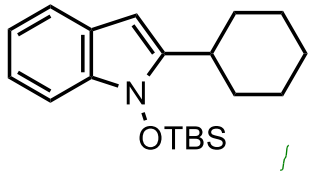
1q'

^{13}C NMR (126 MHz, $CDCl_3$)



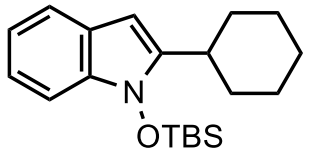
1q'

^{1}H NMR (500 MHz, $CDCl_3$)



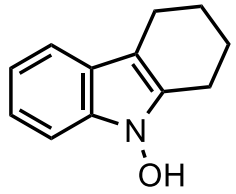
1r'

^{13}C NMR (126 MHz, $CDCl_3$)



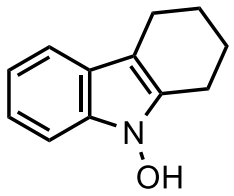
1r'

^{1}H NMR (400 MHz, MeOD)



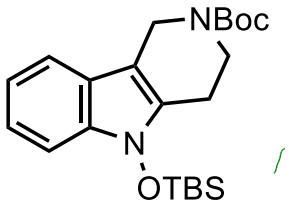
1s

^{13}C NMR (101 MHz, MeOD)



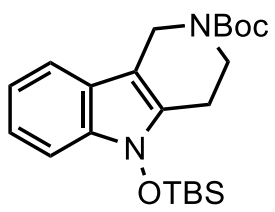
1s

^{1}H NMR (400 MHz, $CDCl_3$)

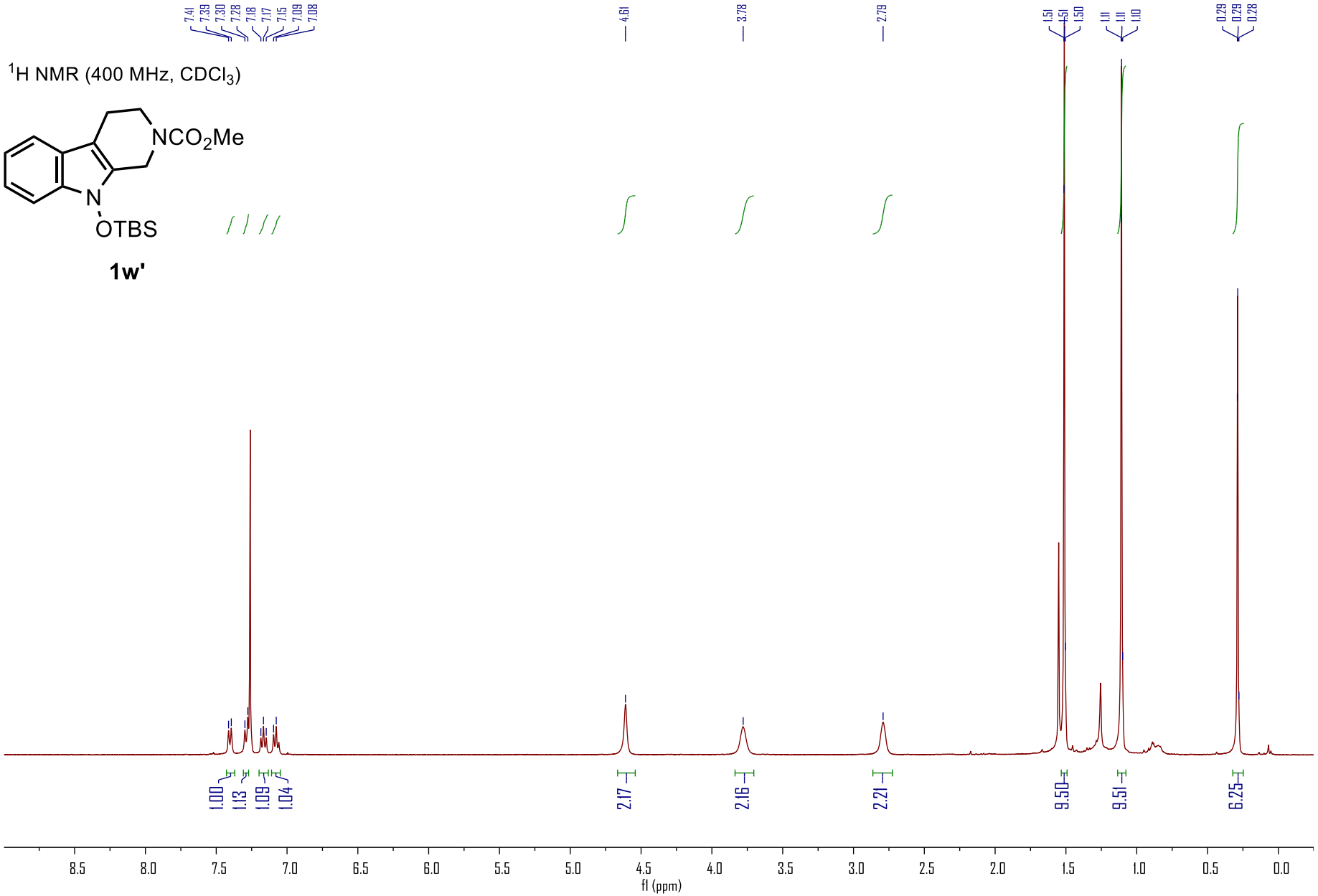


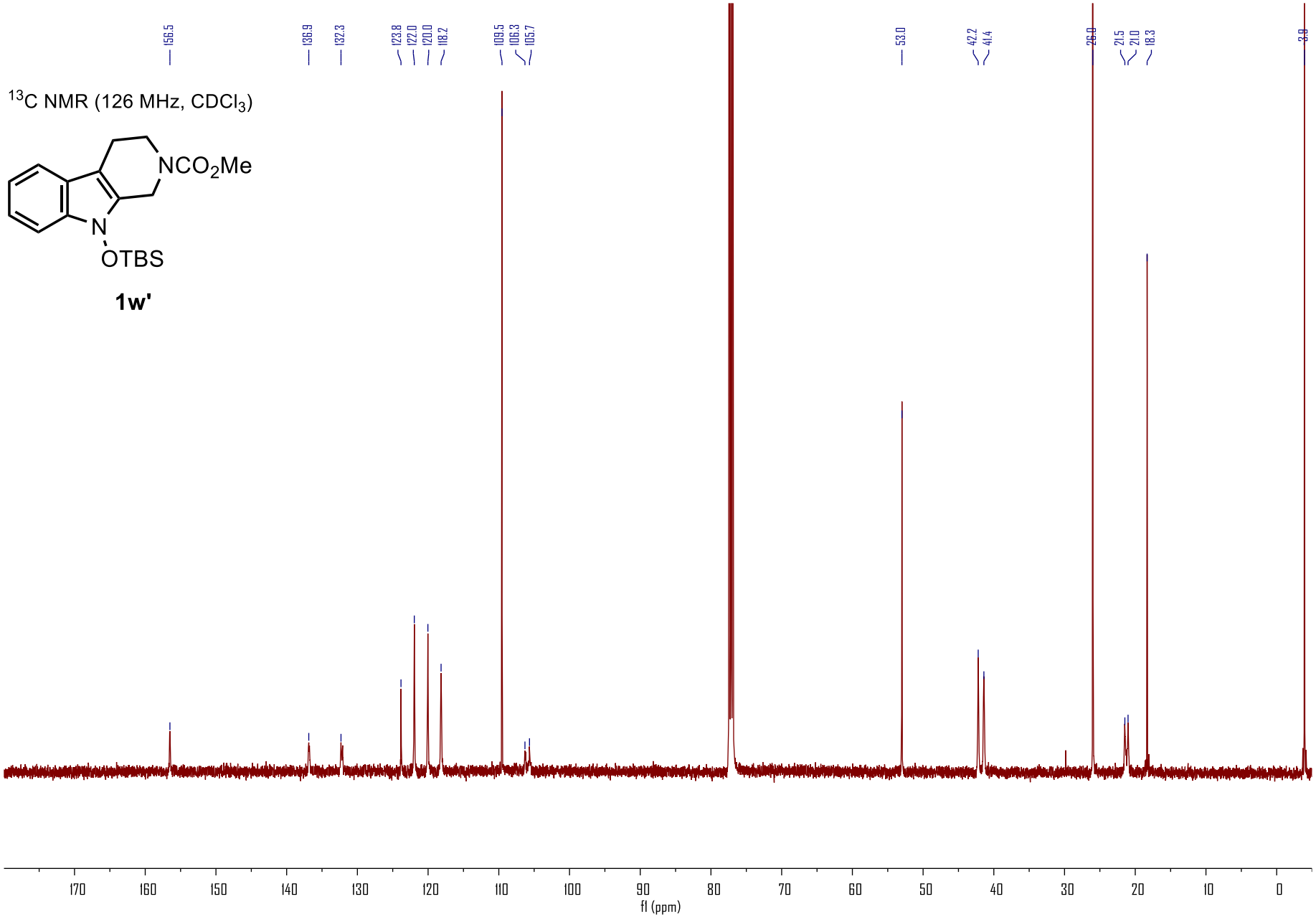
1v'

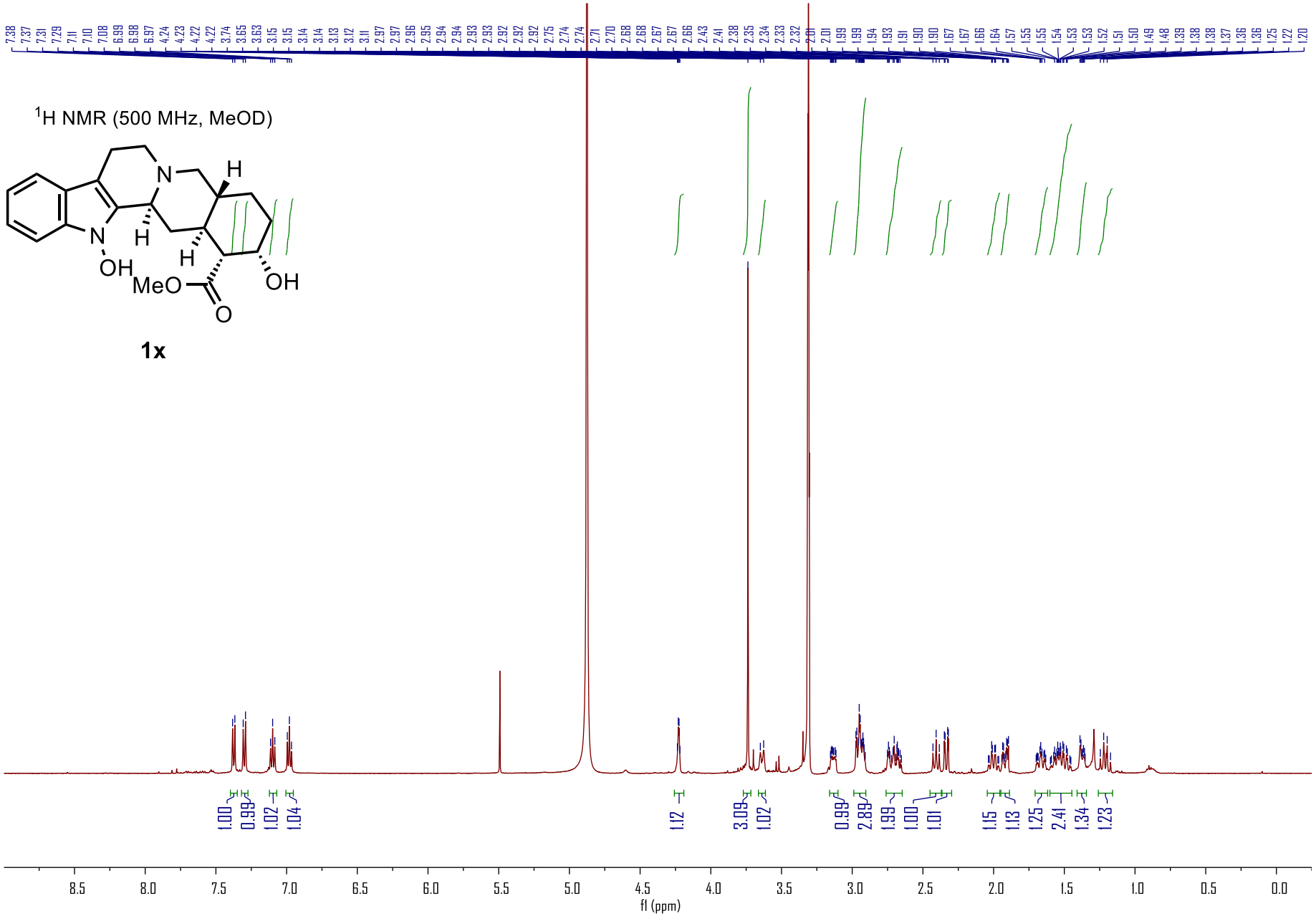
^{13}C NMR (126 MHz, $CDCl_3$)

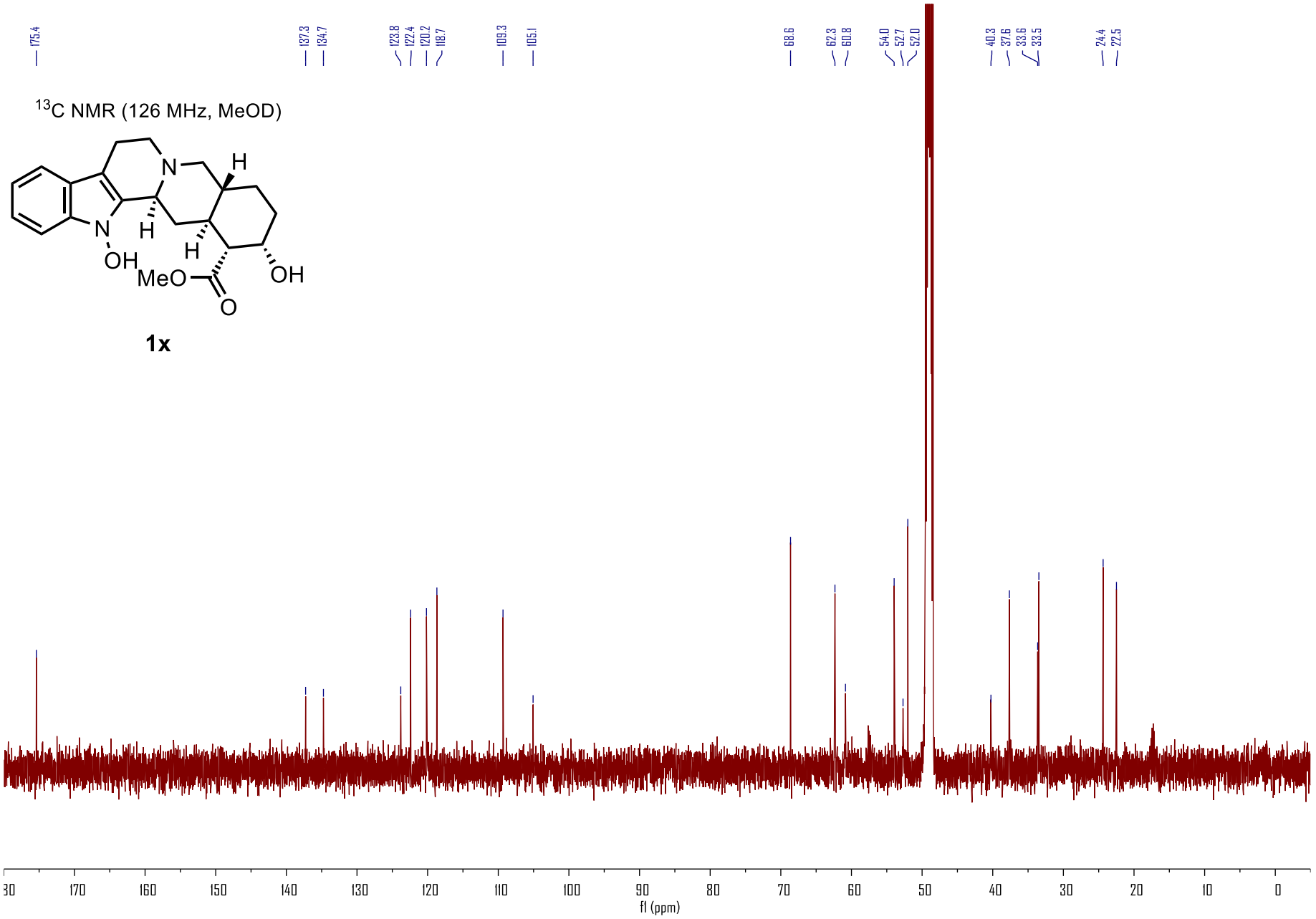


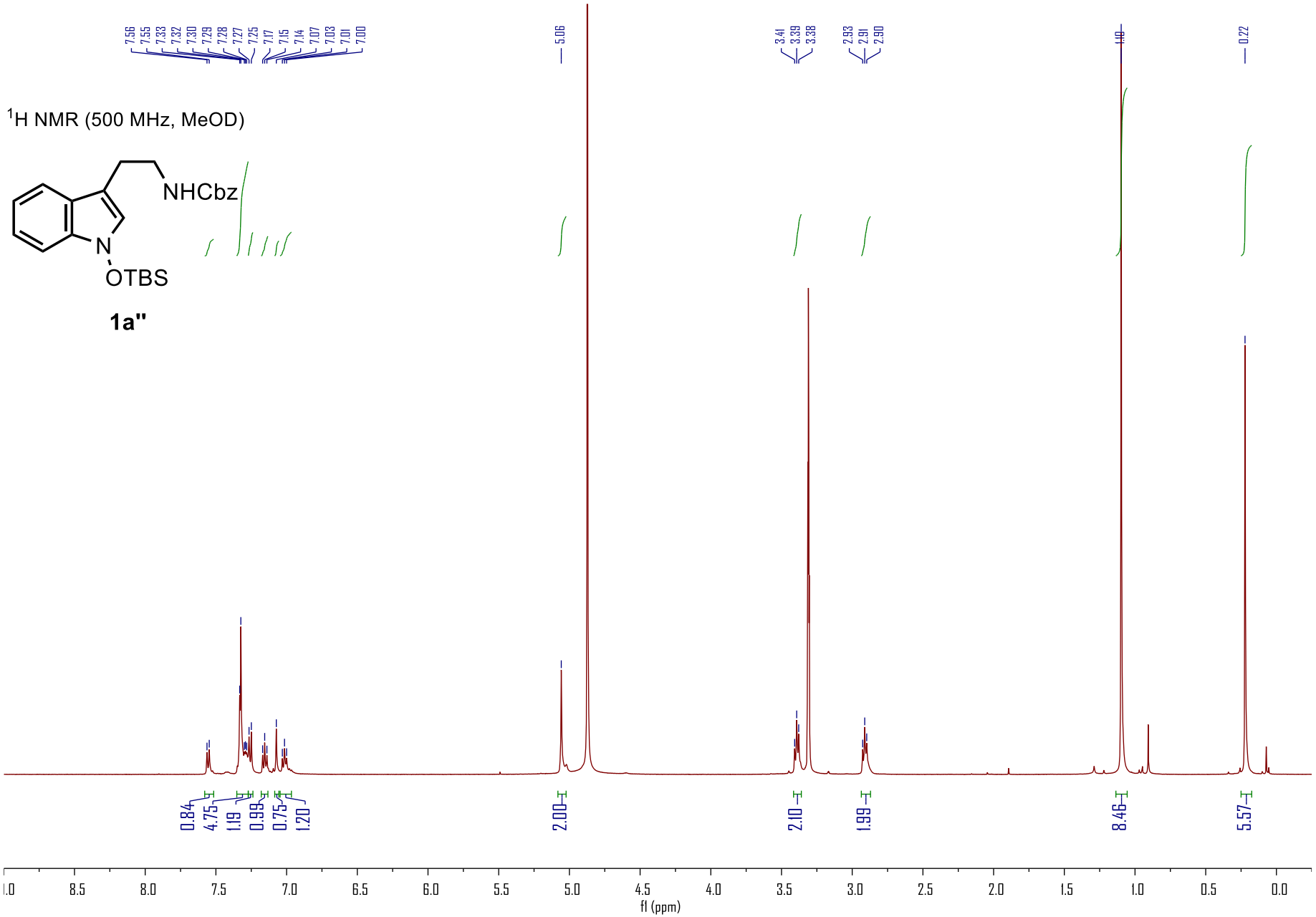
1v'

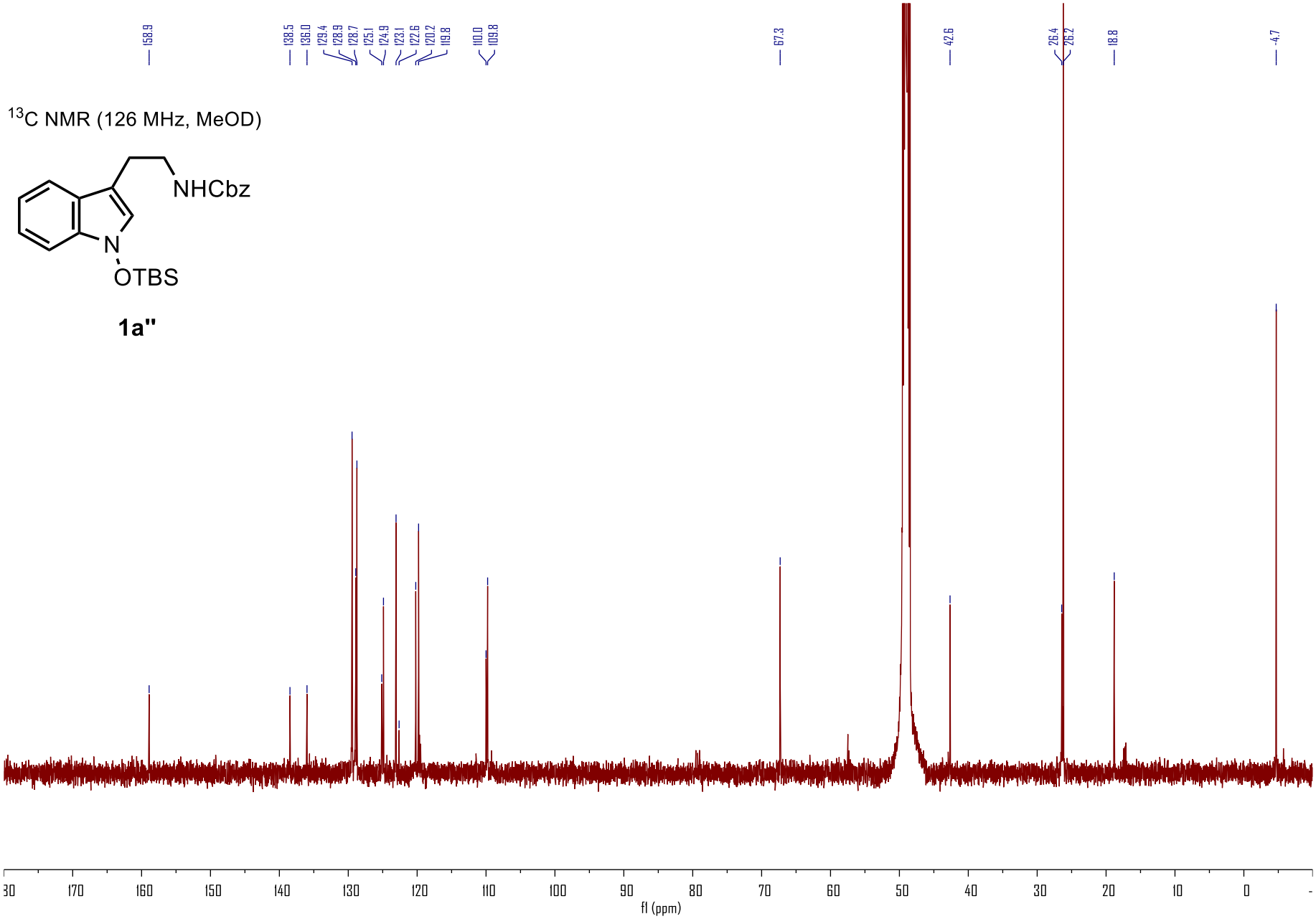

^{1}H NMR (400 MHz, $CDCl_3$)
NCO_2Me
N
OTBS
1w'
7.41
7.39
7.30
7.28
7.18
7.17
7.15
7.09
7.08
4.61
3.78
2.79
1.51
1.51
1.50
1.11
1.11
1.10
0.29
0.29
0.28
1.00
1.13
1.09
1.04
2.17
2.16
2.21
9.50
9.51
6.25
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


156.5
136.9
132.3
123.8
122.0
120.0
118.2
109.5
106.3
105.7
53.0
42.2
41.4
26.0
21.5
21.0
18.3
-3.8
13C NMR (126 MHz, CDCl3)
NCO2Me
N
OTBS
1w'
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

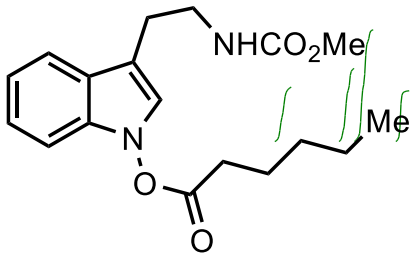

7.38 7.37 7.31 7.29 7.11 7.10 7.08 6.99 6.98 6.97 4.24 4.23 4.22 4.22 3.74 3.65 3.63 3.15 3.15 3.14 3.14 3.13 3.12 3.11 2.97 2.97 2.96 2.95 2.94 2.94 2.93 2.93 2.92 2.92 2.92 2.75 2.74 2.74 2.71 2.70 2.68 2.68 2.67 2.67 2.66 2.43 2.41 2.38 2.35 2.34 2.33 2.32 2.01 2.01 1.99 1.99 1.94 1.93 1.91 1.90 1.90 1.67 1.67 1.66 1.64 1.57 1.55 1.55 1.54 1.53 1.53 1.52 1.51 1.50 1.49 1.48 1.39 1.38 1.38 1.37 1.36 1.36 1.25 1.22 1.20
1H NMR (500 MHz, MeOD)
N
H
N
H
H
OH
MeO
O
OH
1x
1.00 0.99 1.02 1.04 1.12 3.09 1.02 0.99 2.89 1.99 1.00 1.01 1.15 1.13 1.25 2.41 1.34 1.23
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


175.4
137.3
134.7
123.8
122.4
120.2
118.7
109.3
105.1
68.6
62.3
60.8
54.0
52.7
52.0
40.3
37.6
33.6
33.5
24.4
22.5
13C NMR (126 MHz, MeOD)
N
H
N
H
H
OH
MeO
O
OH
1x
f1 (ppm)

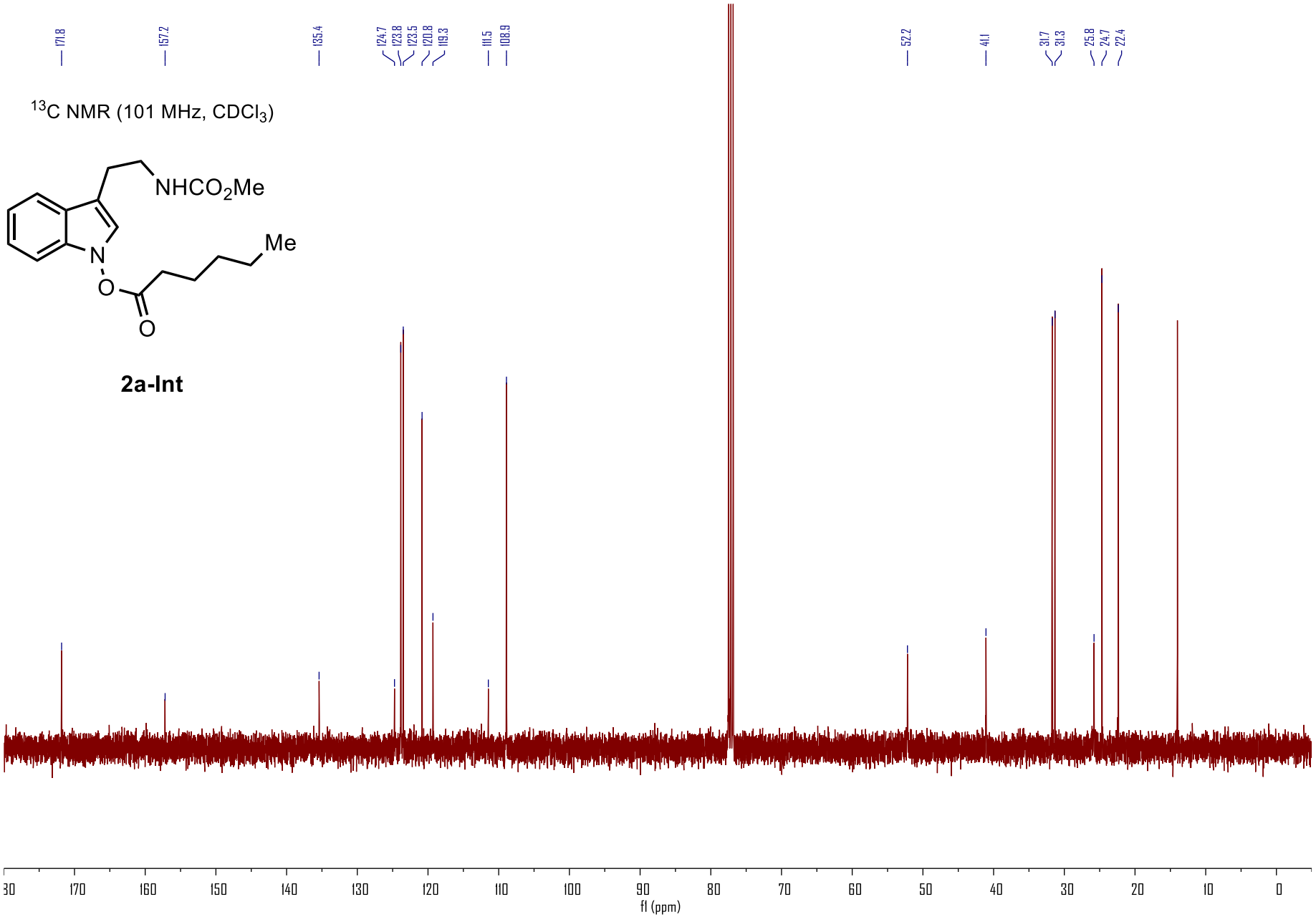

7.56
7.55
7.33
7.32
7.30
7.29
7.28
7.27
7.25
7.17
7.15
7.14
7.07
7.03
7.01
7.00
5.06
3.41
3.39
3.38
2.93
2.91
2.90
1.19
0.22
^{1}H NMR (500 MHz, MeOD)
NHCbz
N
OTBS
1a"
0.84
4.75
1.19
0.98
0.75
1.20
2.00
2.10
1.99
8.46
5.57
f1 (ppm)

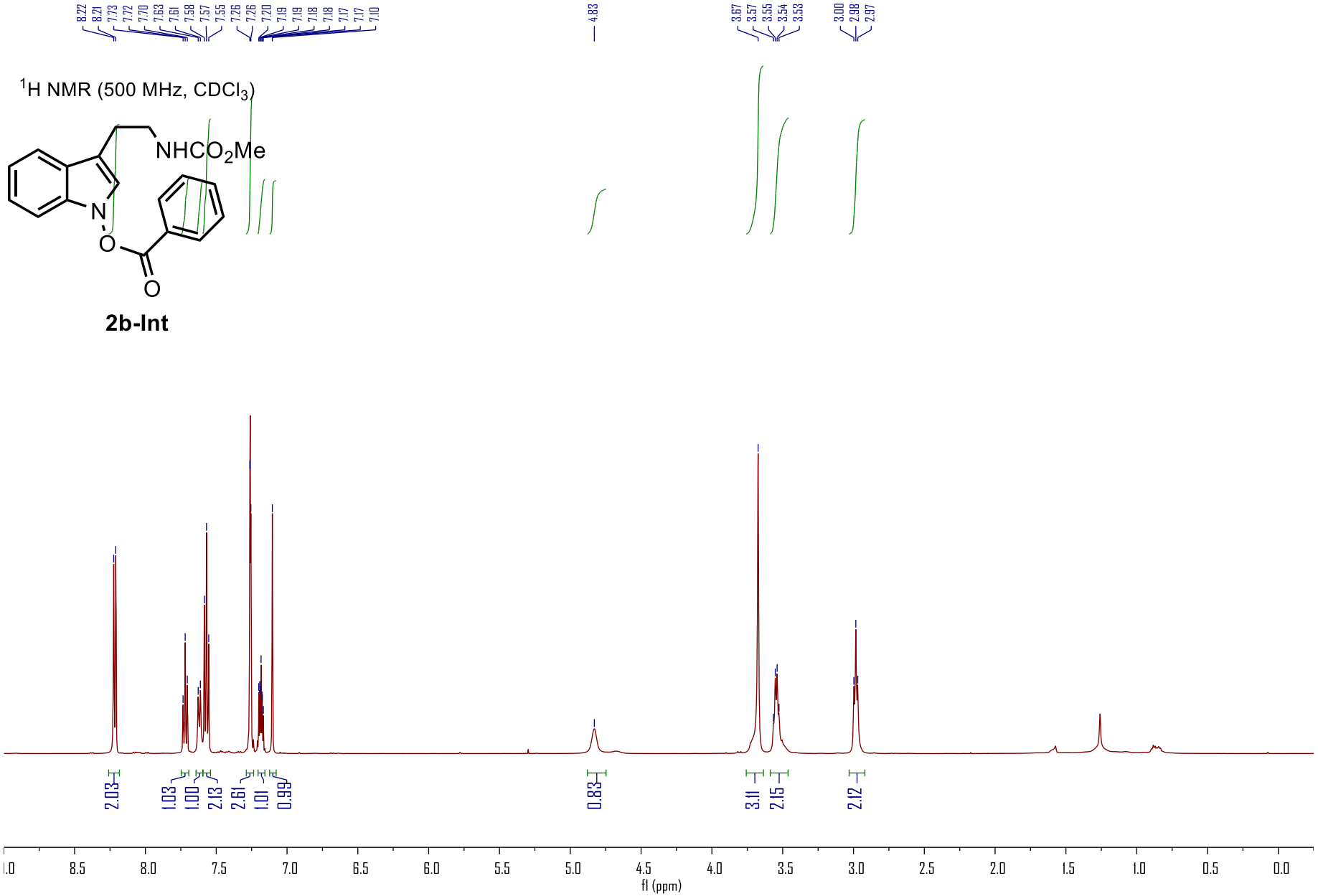

158.9
138.5
136.0
129.4
128.9
128.7
125.1
124.9
123.1
122.6
120.2
119.8
110.0
109.8
67.3
42.6
26.4
26.2
18.8
-4.7
13C NMR (126 MHz, MeOD)
NHCbz
N
OTBS
1a"
f1 (ppm)

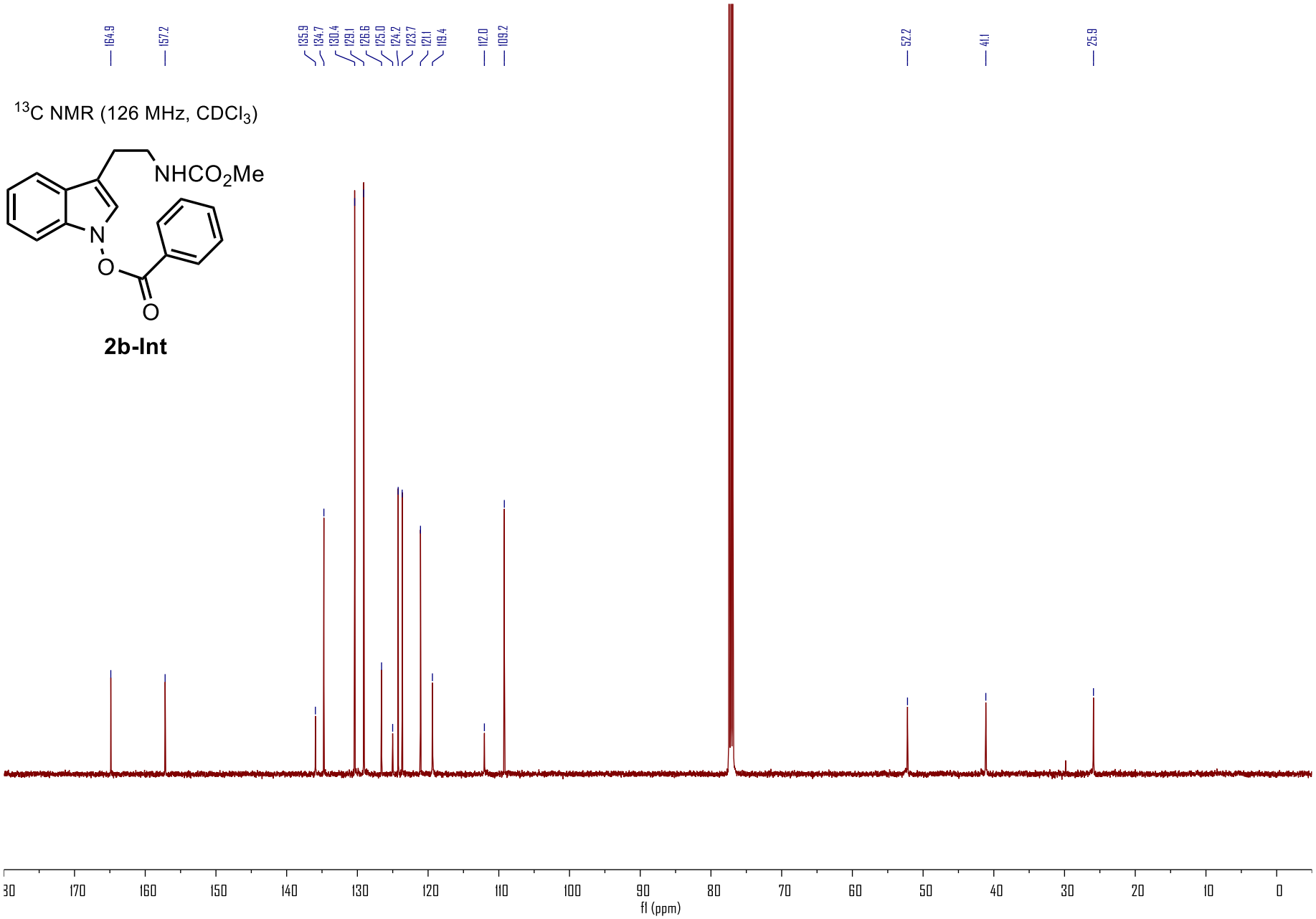
^{1}H NMR (400 MHz, $CDCl_3$)

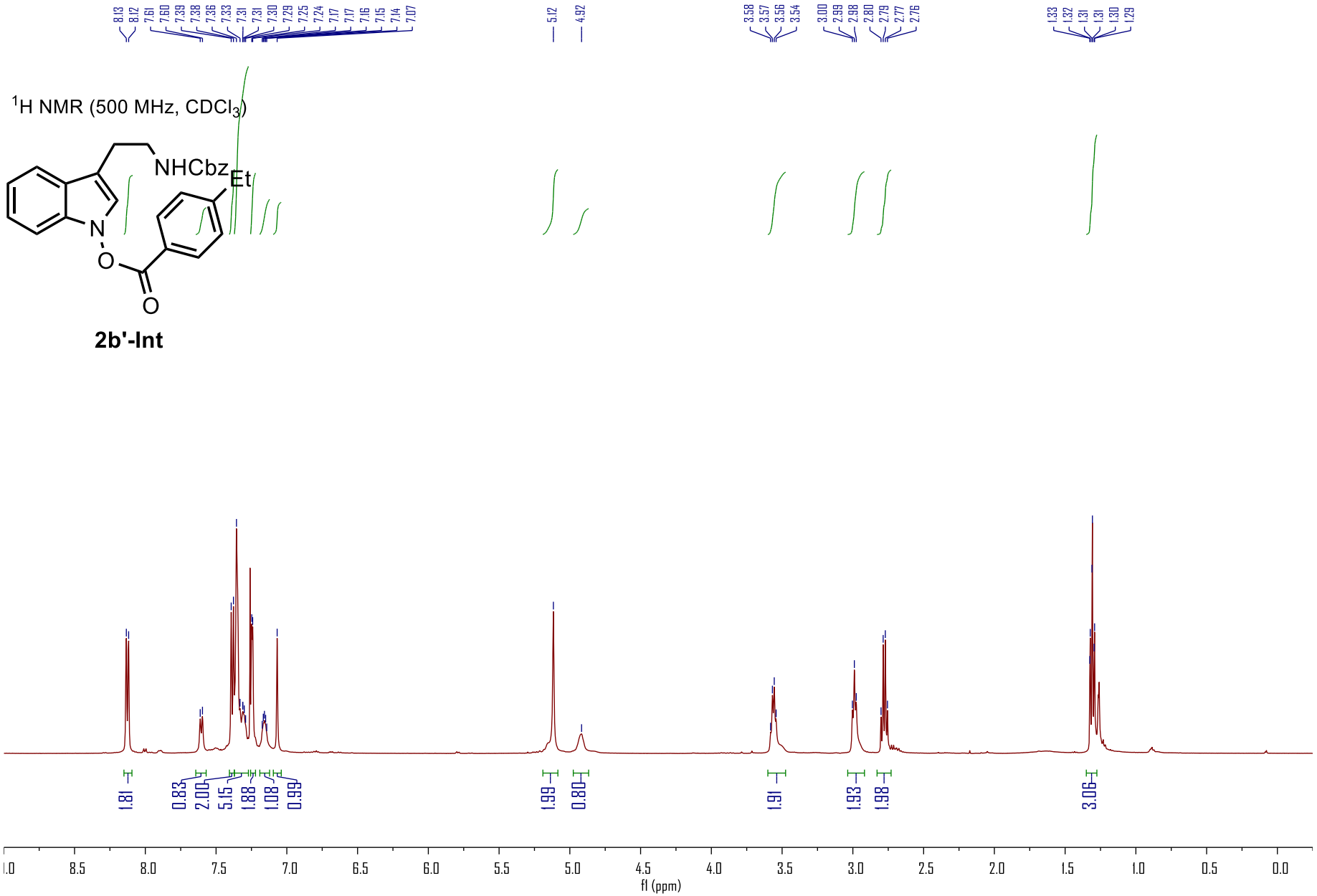


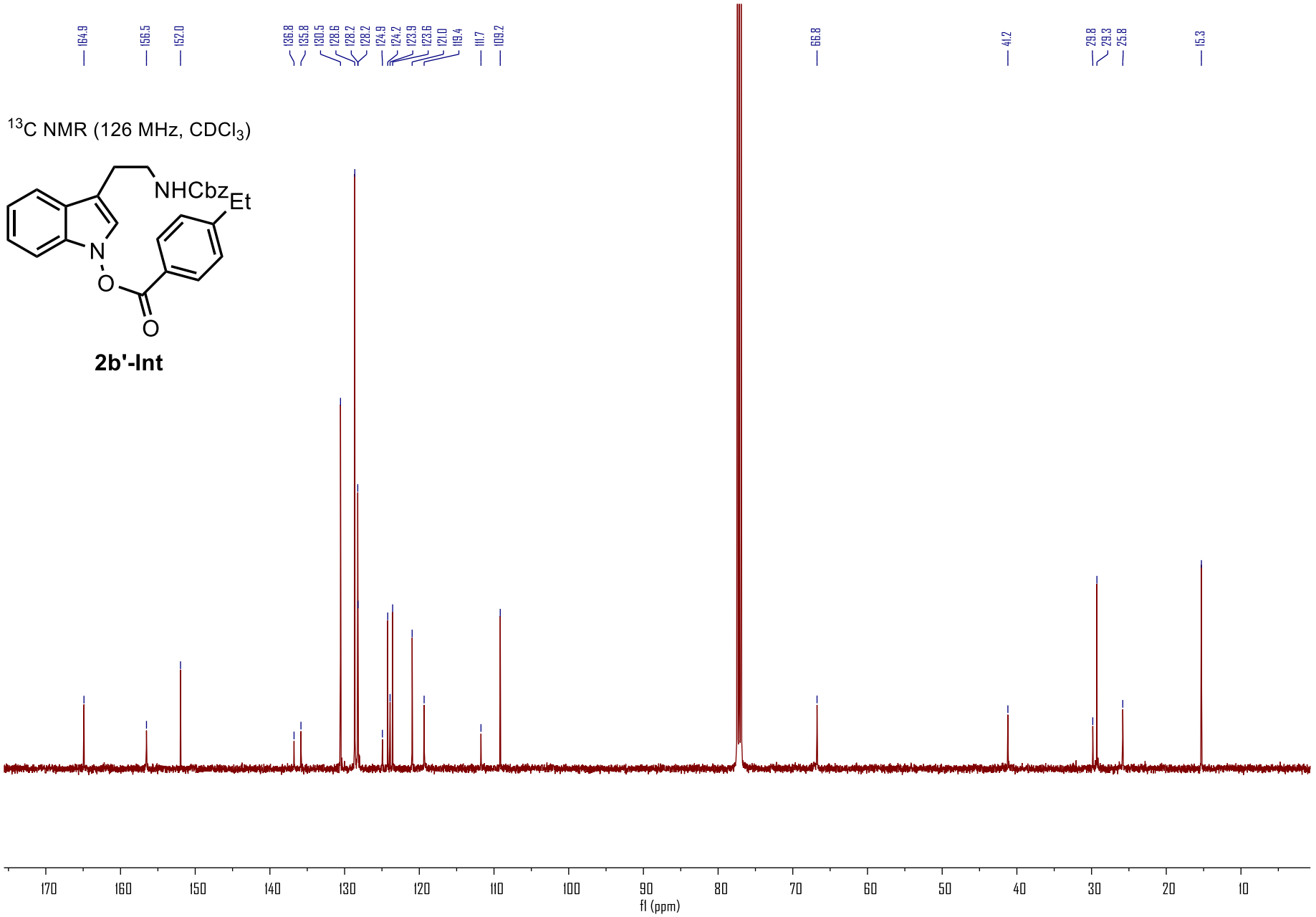
2a-Int

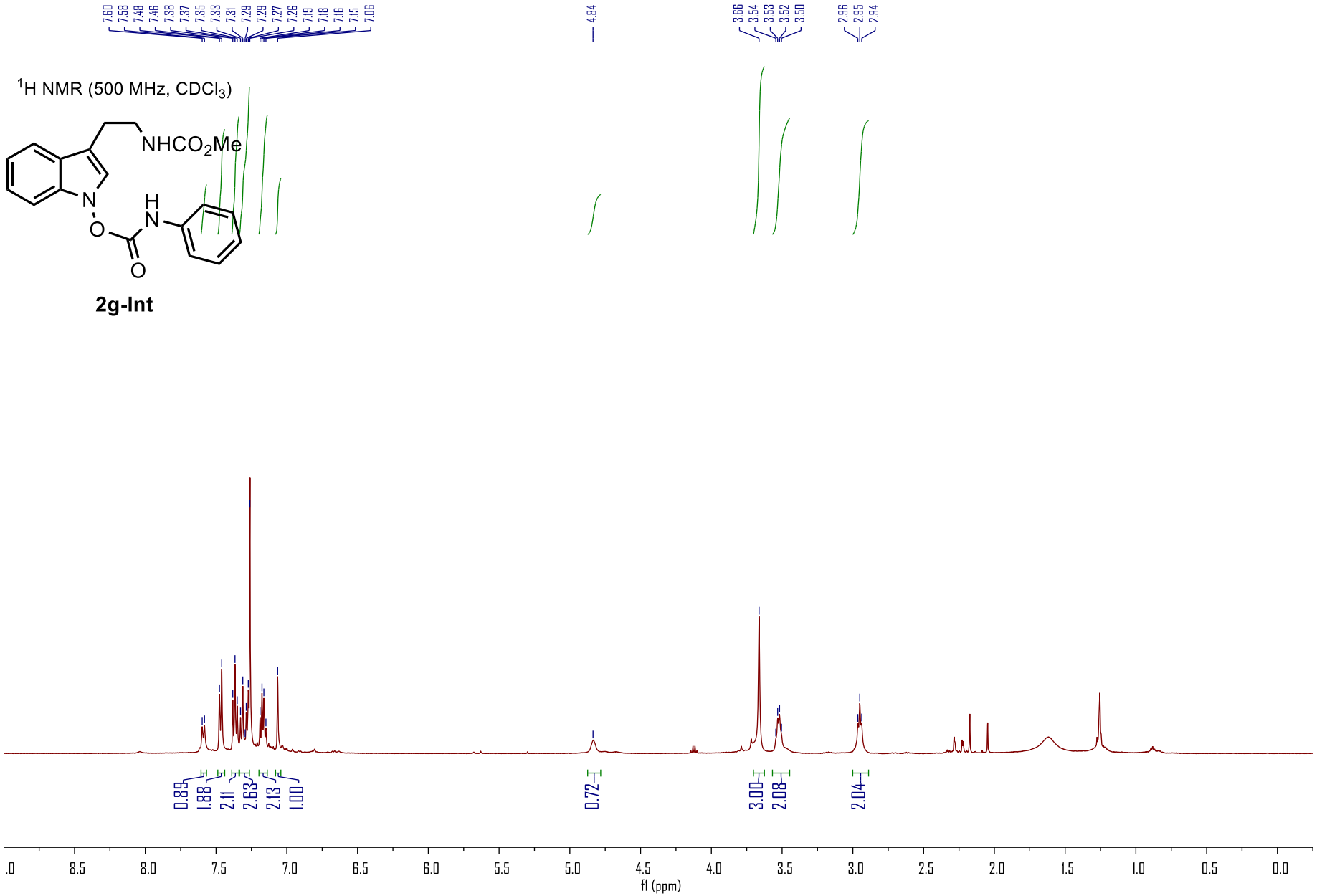

171.8
157.2
135.4
124.7
123.8
123.5
120.8
119.3
111.5
108.9
52.2
41.1
31.7
31.3
25.8
24.7
22.4
13C NMR (101 MHz, CDCl3)
NHCO2Me
Me
N
O
O
2a-Int
f1 (ppm)

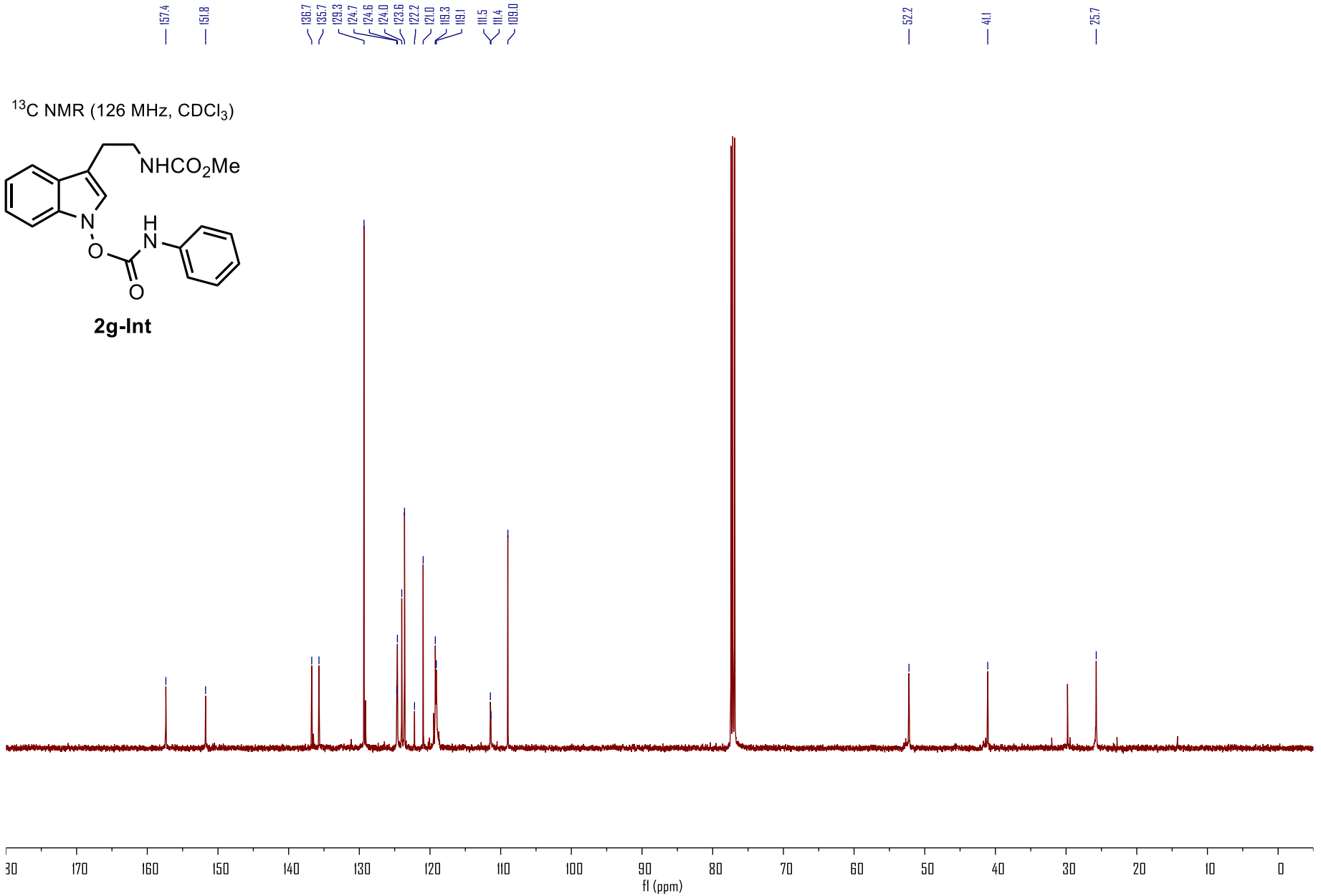

8.22
8.21
7.73
7.72
7.70
7.63
7.61
7.58
7.57
7.55
7.26
7.26
7.20
7.19
7.19
7.18
7.18
7.17
7.17
7.10
4.83
3.67
3.57
3.55
3.54
3.53
3.00
2.98
2.97
1H NMR (500 MHz, CDCl3)
NHCO2Me
N
O
O
2b-Int
2.03
1.03
1.00
2.13
2.61
1.01
0.99
0.83
3.11
2.15
2.12
f1 (ppm)

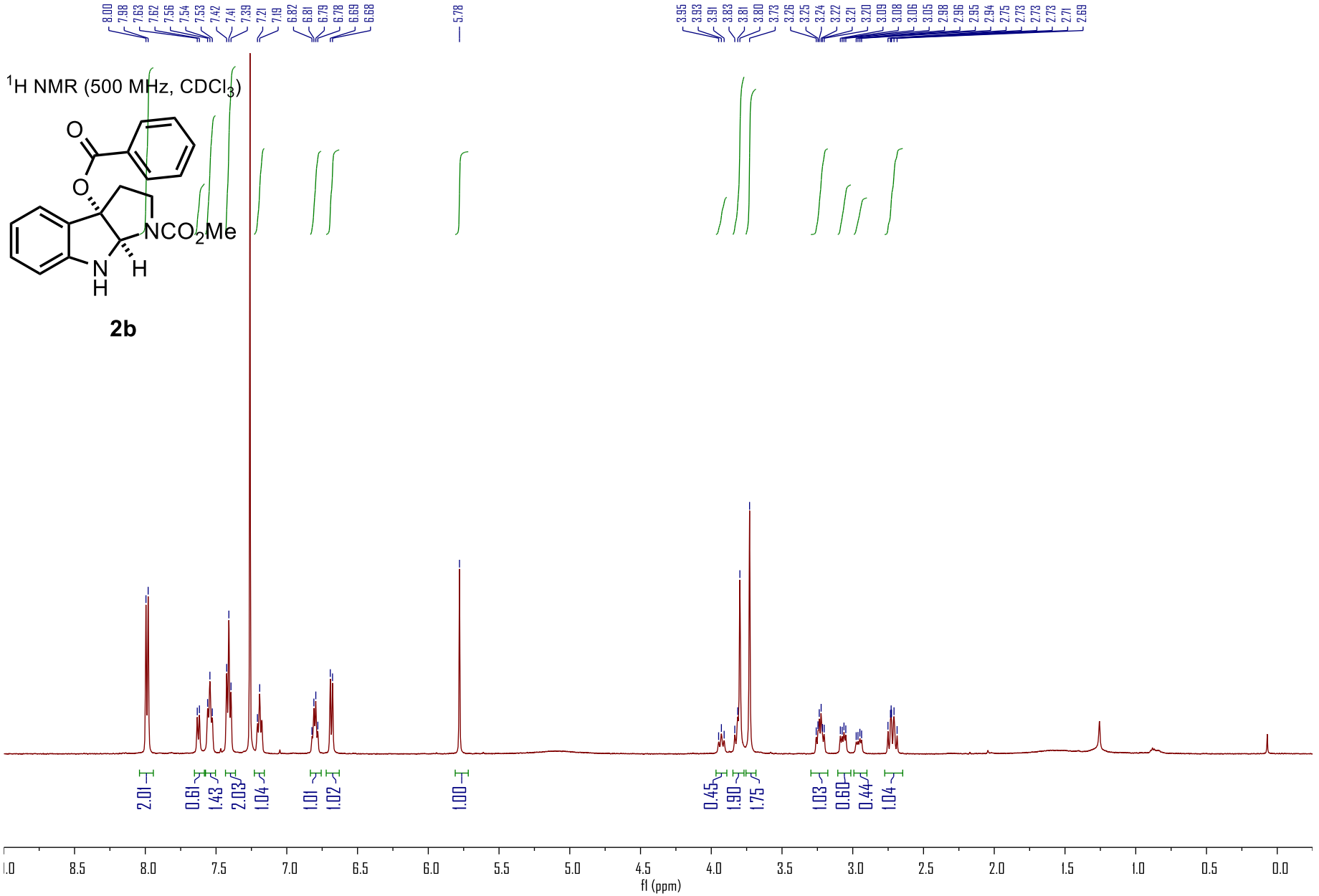

164.9
157.2
135.9
134.7
130.4
129.1
126.6
125.0
124.2
123.7
121.1
119.4
112.0
109.2
52.2
41.1
25.9
^{13}C NMR (126 MHz, $CDCl_3$)
NHCO$_2$Me
N
O
O
2b-Int
f1 (ppm)

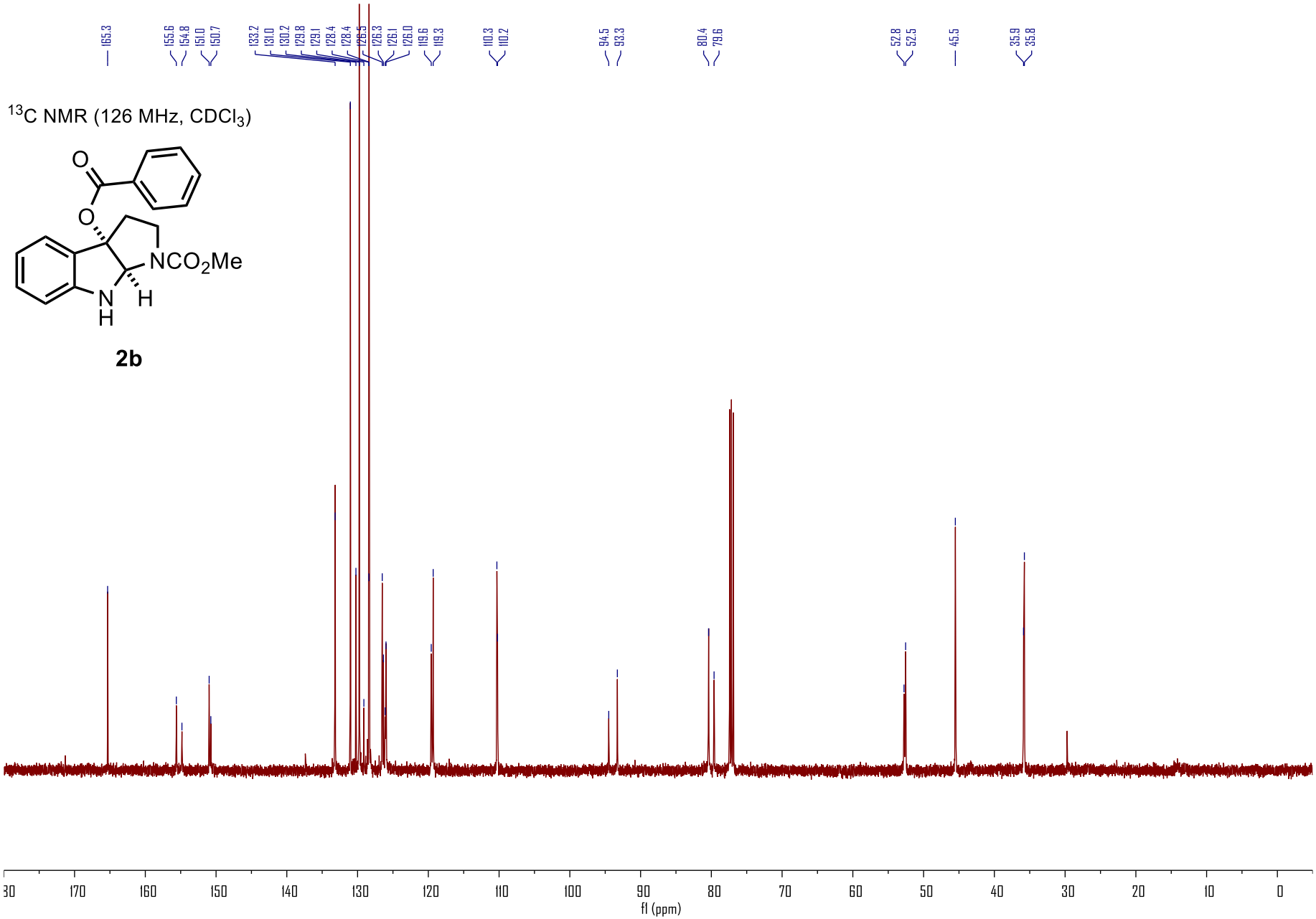

8.13
8.12
7.61
7.60
7.39
7.38
7.36
7.33
7.31
7.31
7.30
7.29
7.25
7.24
7.17
7.17
7.16
7.15
7.14
7.07
5.12
4.92
3.58
3.57
3.56
3.54
3.00
2.99
2.98
2.80
2.79
2.77
2.76
1.33
1.32
1.31
1.31
1.30
1.29
^{1}H NMR (500 MHz, CDCl$_3$)
NHCbz
Et
N
O
O
2b'-Int
1.81
0.83
2.00
5.15
1.88
1.08
0.99
1.99
0.80
1.91
1.93
1.98
3.06
f1 (ppm)

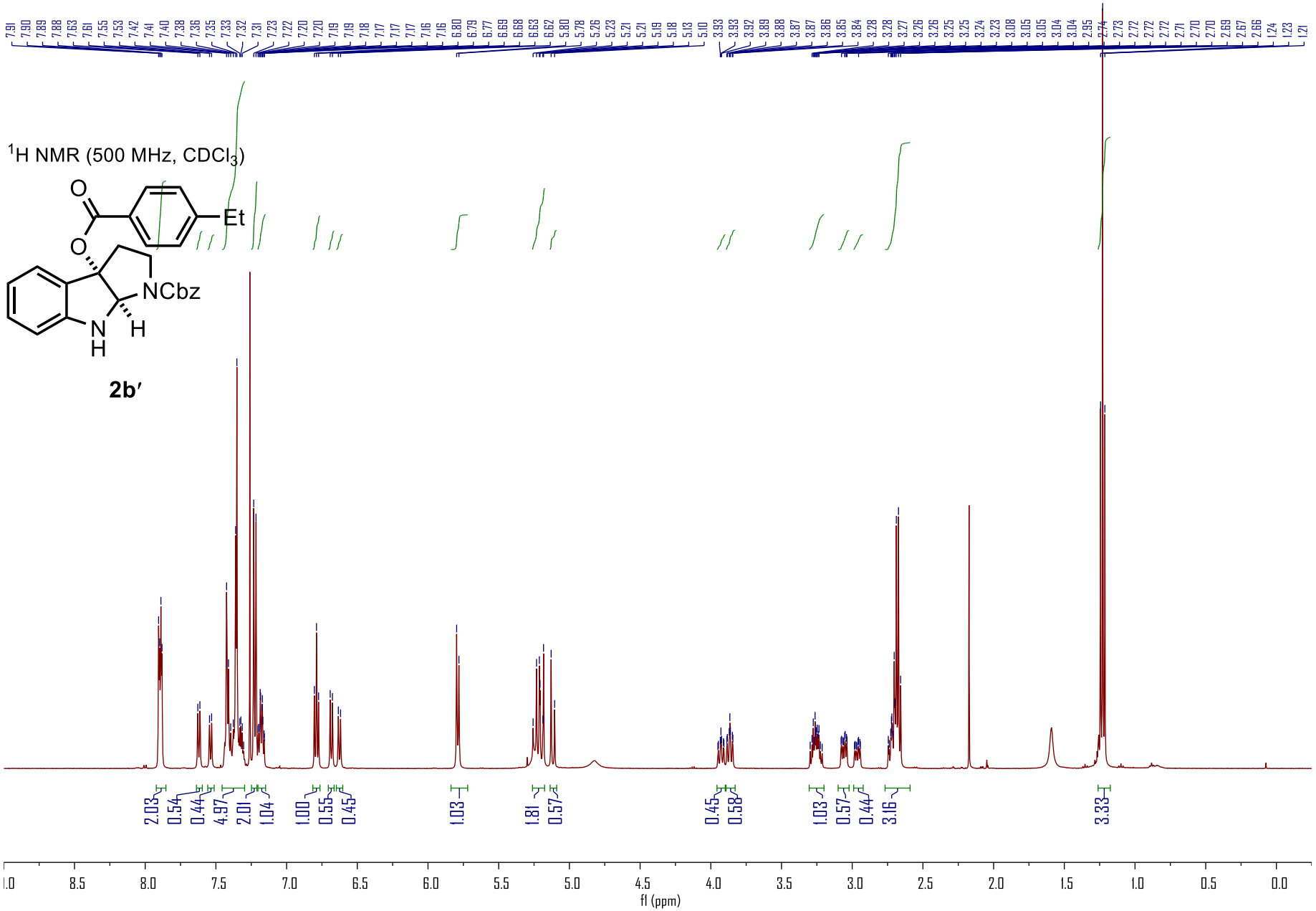

164.9
156.5
152.0
136.8
135.8
130.5
128.6
128.2
128.2
124.9
124.2
123.9
123.6
121.0
119.4
111.7
109.2
66.8
41.2
29.8
29.3
25.8
15.3
^{13}C NMR (126 MHz, $CDCl_3$)
NHCbz
Et
N
O
O
2b'-Int
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

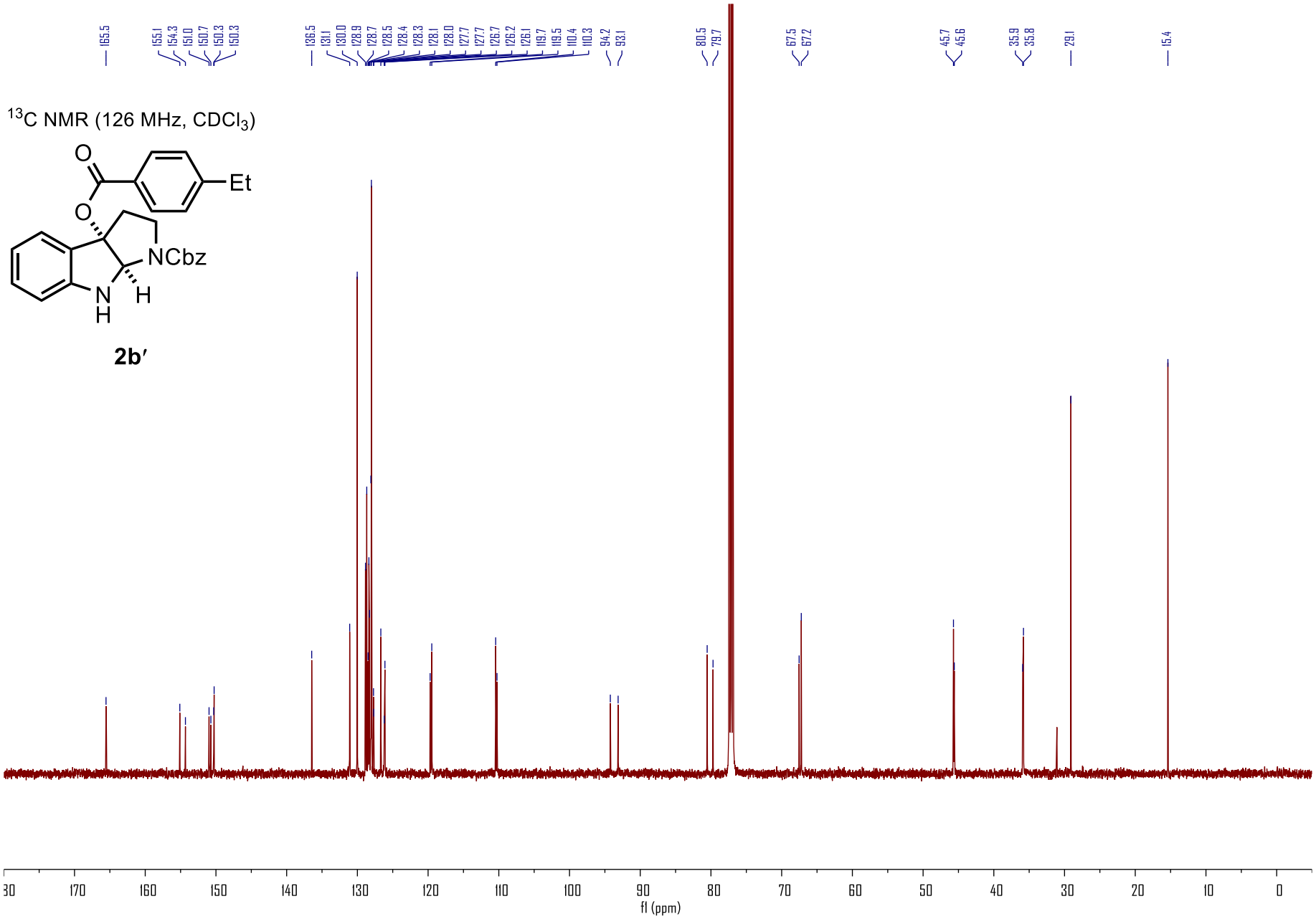

7.60
7.58
7.48
7.46
7.38
7.37
7.35
7.33
7.31
7.29
7.29
7.27
7.26
7.19
7.18
7.16
7.15
7.06
4.84
3.66
3.54
3.53
3.52
3.50
2.96
2.95
2.94
^{1}H NMR (500 MHz, $CDCl_3$)
$NHCO_2Me$
N
O
H
N
O
2g-Int
0.89
1.88
2.11
2.63
2.13
1.00
0.72
3.00
2.08
2.04
f1 (ppm)

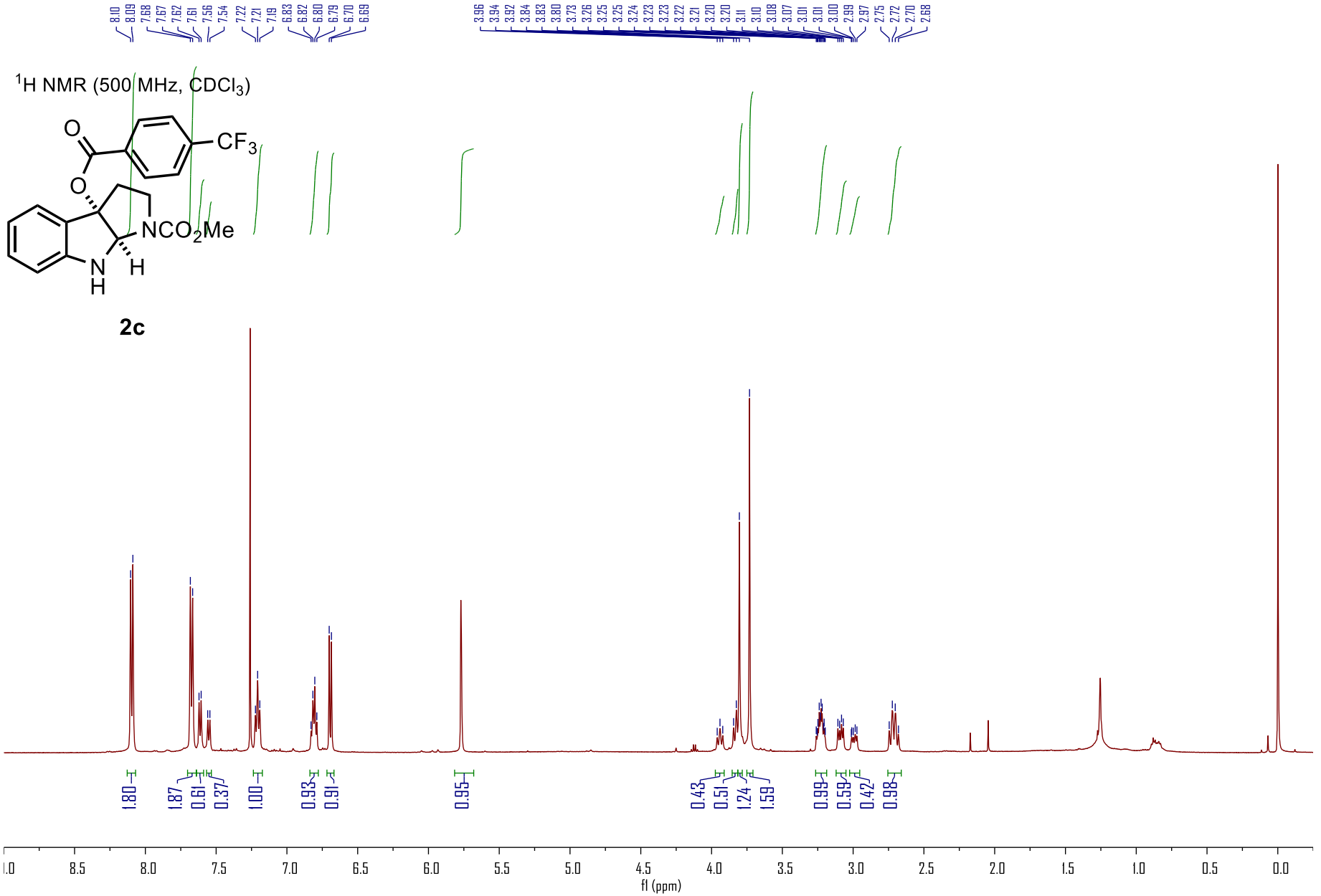

157.4
151.8
136.7
135.7
129.3
124.7
124.6
124.0
123.6
122.2
121.0
119.3
119.1
111.5
111.4
109.0
52.2
44.1
25.7
^{13}C NMR (126 MHz, $CDCl_3$)
NHCO$_2$Me
N
O
H
N
O
2g-Int
f1 (ppm)


^{1}H NMR (500 MHz, $CDCl_3$)
NCO$_2$Me
N
H
H
2b
8.00
7.98
7.63
7.62
7.56
7.54
7.53
7.42
7.41
7.39
7.21
7.19
6.82
6.81
6.79
6.78
6.69
6.68
5.78
3.95
3.93
3.91
3.83
3.81
3.80
3.73
3.28
3.25
3.24
3.22
3.21
3.20
3.09
3.08
3.06
3.05
2.98
2.96
2.95
2.94
2.75
2.73
2.73
2.73
2.71
2.69
2.01
0.61
1.43
2.03
1.04
1.01
1.02
1.00
0.45
1.90
1.75
1.03
0.60
0.44
1.04
f1 (ppm)

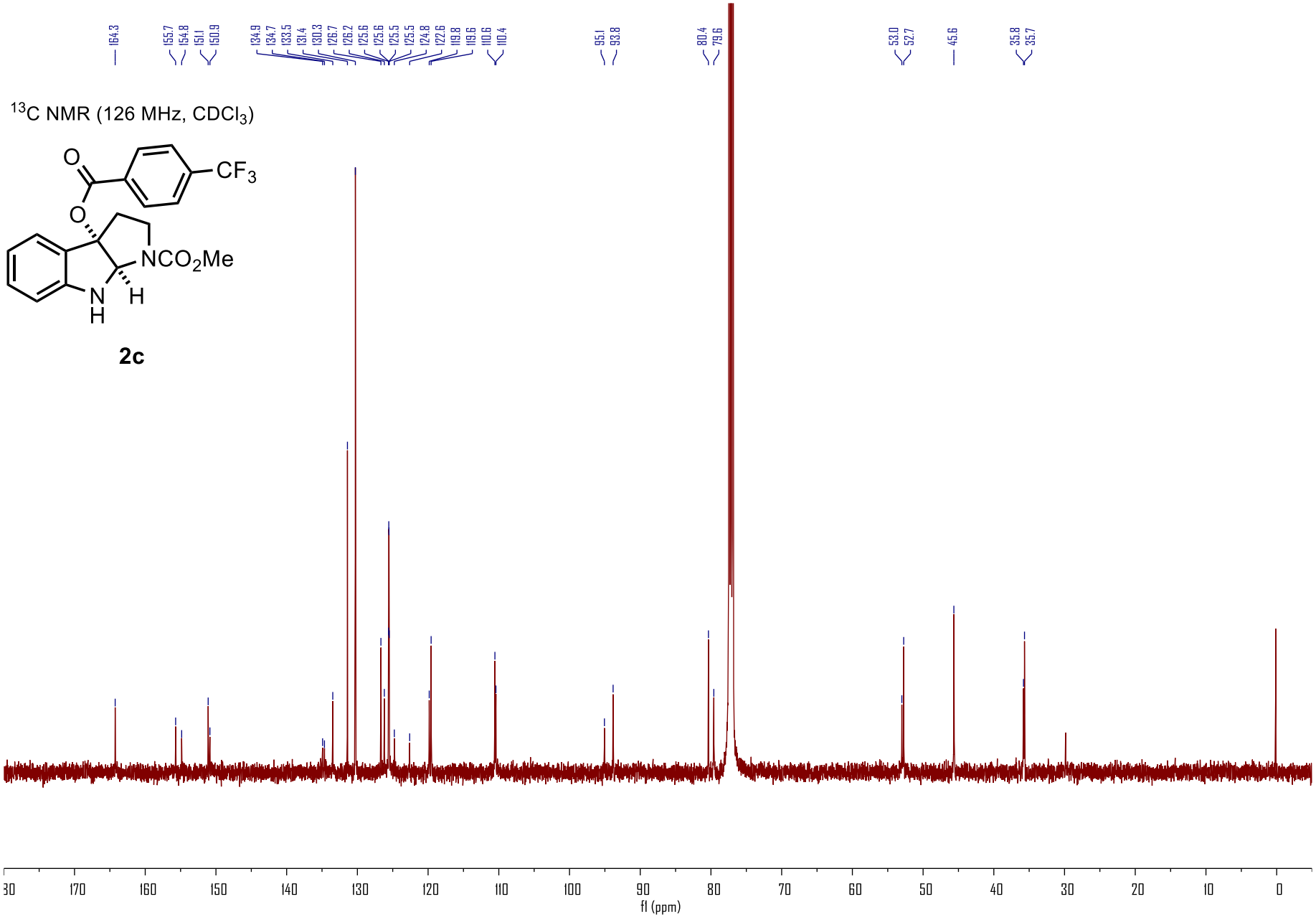

165.3
155.6
154.8
151.0
150.7
133.2
131.0
130.2
129.8
129.1
128.4
128.4
128.5
126.3
126.1
126.0
119.6
119.3
110.3
110.2
94.5
93.3
80.4
79.6
52.8
52.5
45.5
35.9
35.8
13C NMR (126 MHz, CDCl3)
O
O
NCO2Me
N
H
H
2b
f1 (ppm)


^{1}H NMR (500 MHz, CDCl$_3$)
Et
NCbz
N
H
H
2b′
f1 (ppm)

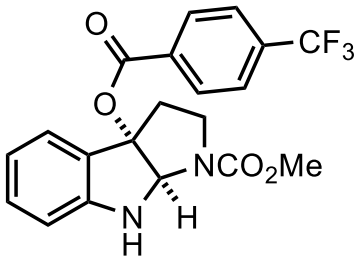

165.5
155.1
154.3
151.0
150.7
150.3
150.3
136.5
131.1
130.0
128.9
128.7
128.5
128.4
128.3
128.1
128.0
127.7
127.7
126.7
126.2
126.1
119.7
119.5
110.4
110.3
94.2
93.1
80.5
79.7
67.5
67.2
45.7
45.6
35.9
35.8
29.1
15.4
13C NMR (126 MHz, CDCl3)
O
O
Et
NCbz
N
H
H
2b′
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.10
8.09
7.68
7.67
7.62
7.61
7.56
7.54
7.22
7.21
7.19
6.83
6.82
6.80
6.79
6.70
6.69
3.96
3.94
3.92
3.84
3.83
3.80
3.73
3.26
3.25
3.25
3.24
3.23
3.23
3.22
3.21
3.20
3.20
3.11
3.10
3.08
3.07
3.01
3.01
3.00
2.99
2.97
2.75
2.72
2.70
2.68
^{1}H NMR (500 MHz, $CDCl_3$)
O
O
CF_3
NCO_2Me
N
H
H
1.80
1.87
0.61
0.37
1.00
0.93
0.91
0.95
0.43
0.51
1.24
1.59
0.99
0.59
0.42
0.98
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

2c

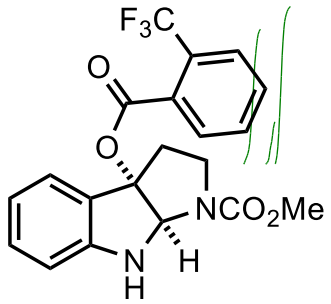

164.3
155.7
154.8
151.1
150.9
134.9
134.7
133.5
131.4
130.3
126.7
126.2
125.6
125.6
125.5
125.5
124.8
122.6
119.8
119.6
110.6
110.4
95.1
93.8
80.4
79.6
53.0
52.7
45.6
35.8
35.7
^{13}C NMR (126 MHz, $CDCl_3$)
O
O
CF_3
NCO_2Me
N
H
H
2c
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

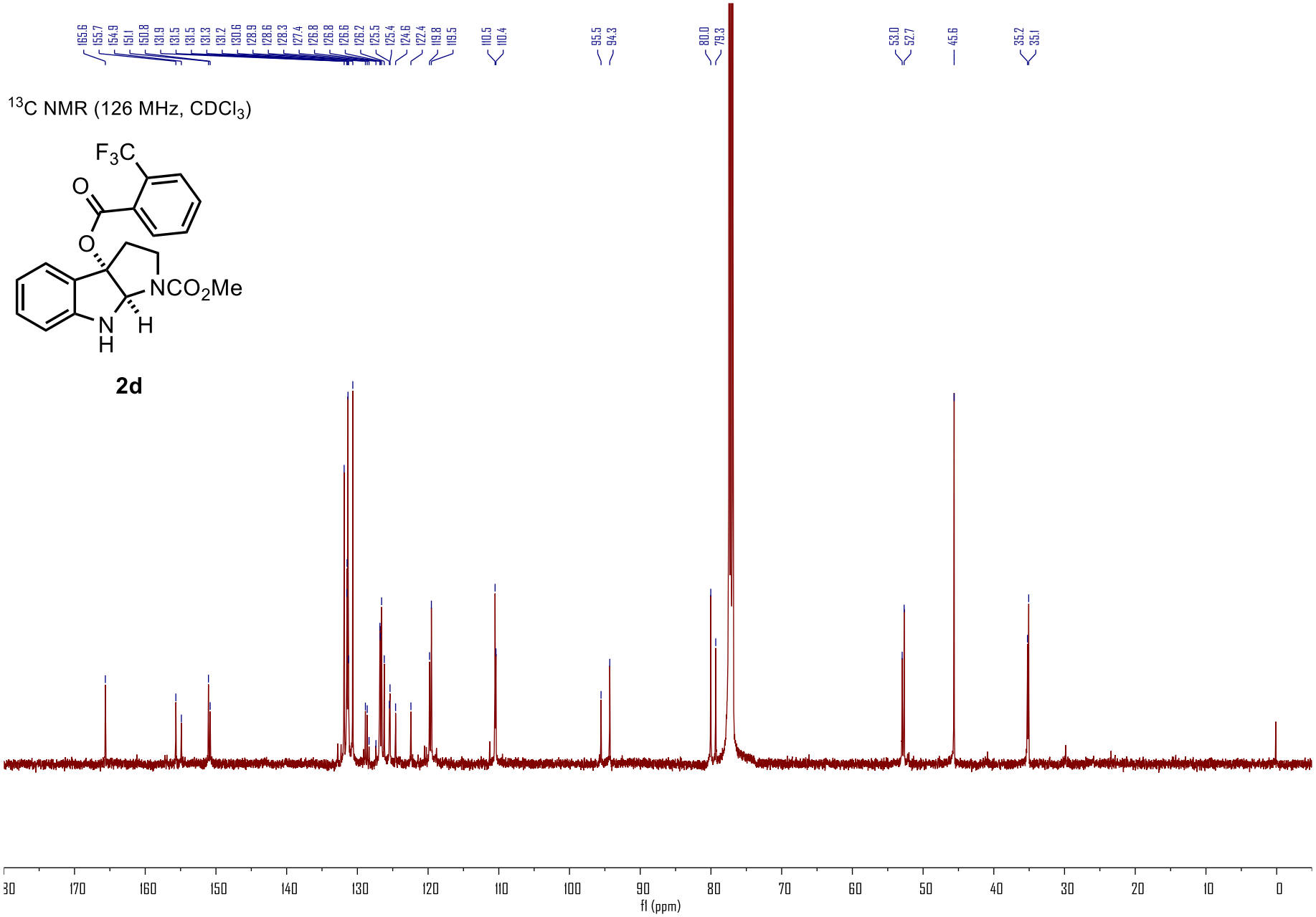


2c

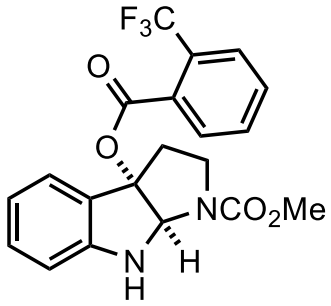
^{1}H NMR (500 MHz, $CDCl_3$)



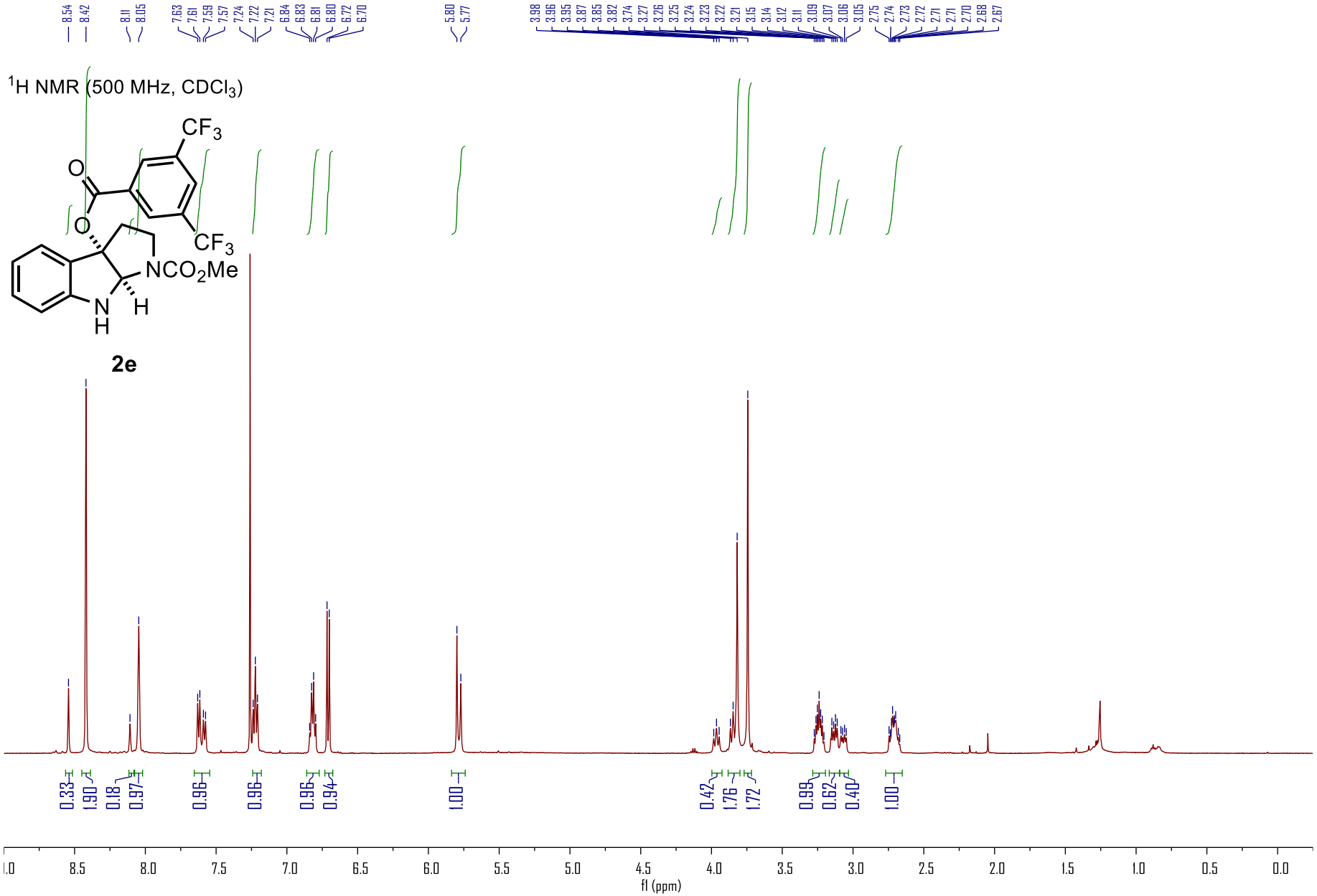
2d

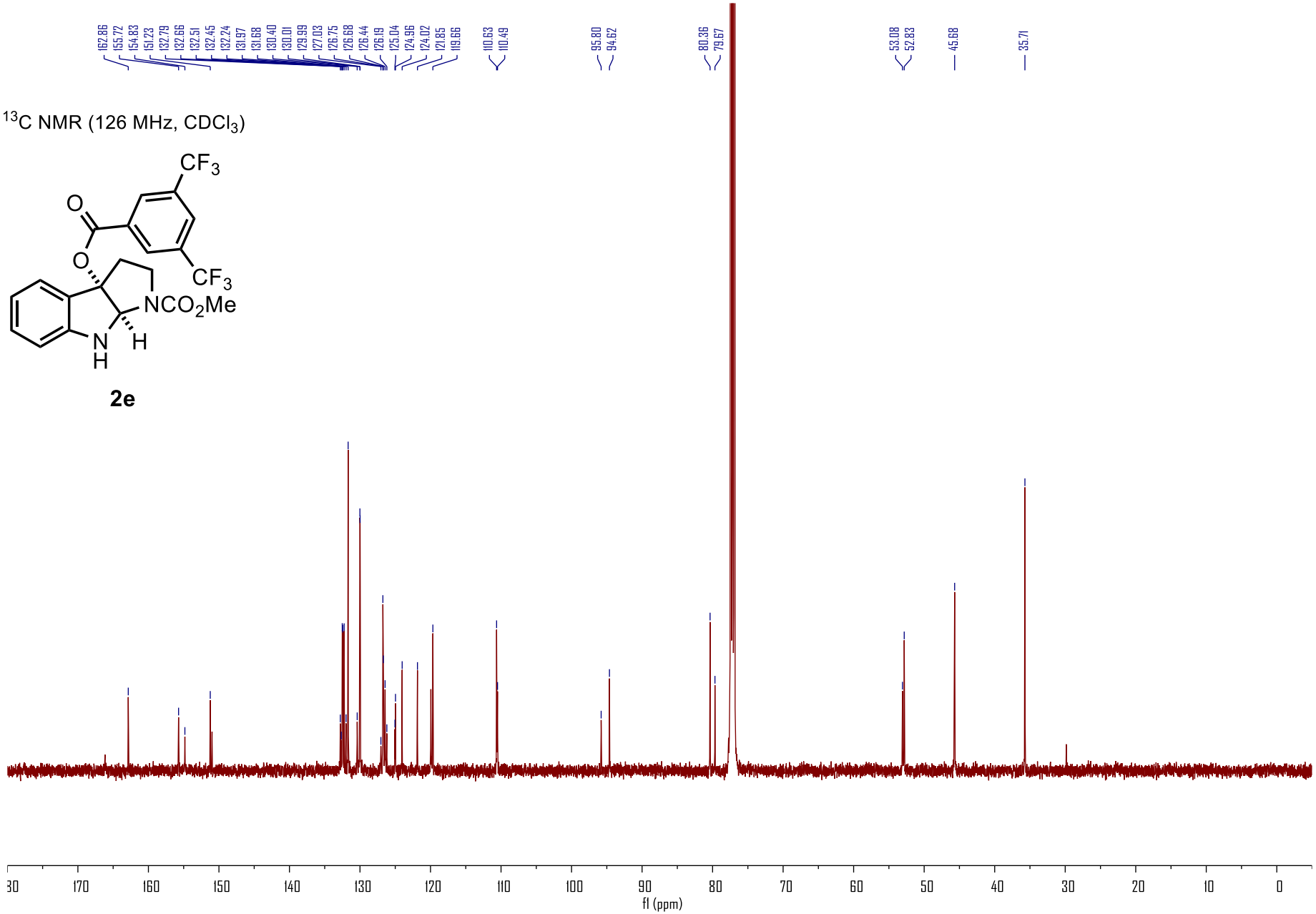

165.6
155.7
154.9
151.1
150.8
131.9
131.5
131.5
131.3
131.2
130.6
128.9
128.6
128.3
127.4
126.8
126.8
126.6
126.2
125.5
125.4
124.6
122.4
119.8
119.5
110.5
110.4
95.5
94.3
80.0
79.3
53.0
52.7
45.6
35.2
35.1
^{13}C NMR (126 MHz, $CDCl_3$)
F_3C
O
O
NCO_2Me
N
H
H
2d
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)



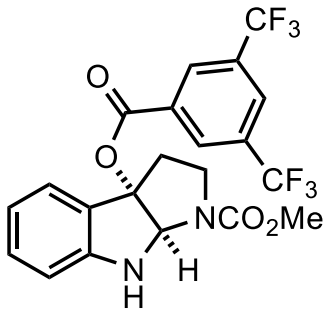
2d


^{1}H NMR (500 MHz, $CDCl_3$)
CF_3
O
O
CF_3
NCO_2Me
N
H
H
2e
8.54
8.42
8.11
8.05
7.63
7.61
7.59
7.57
7.24
7.22
7.21
6.84
6.83
6.81
6.80
6.72
6.70
5.80
5.77
3.98
3.96
3.95
3.87
3.85
3.82
3.74
3.27
3.26
3.25
3.24
3.23
3.22
3.21
3.15
3.14
3.12
3.11
3.09
3.07
3.06
3.05
2.75
2.74
2.73
2.72
2.71
2.71
2.70
2.68
2.67
0.33
1.90
0.18
0.97
0.96
0.96
0.96
0.94
1.00
0.42
1.76
1.72
0.99
0.62
0.40
1.00
f1 (ppm)


162.86
155.72
154.83
151.23
132.79
132.66
132.51
132.45
132.24
131.97
131.68
130.40
130.01
129.99
127.03
126.75
126.68
126.44
126.19
125.04
124.96
124.02
121.85
119.66
110.63
110.48
95.80
94.62
80.36
79.67
53.08
52.83
45.68
35.71
^{13}C NMR (126 MHz, $CDCl_3$)
CF_3
O
O
CF_3
NCO_2Me
N
H
H
f1 (ppm)

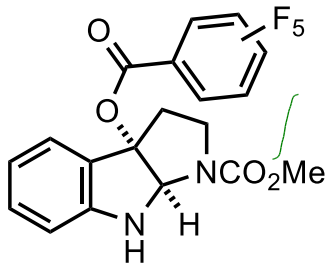
2e

^{19}F NMR (471 MHz, $CDCl_3$)

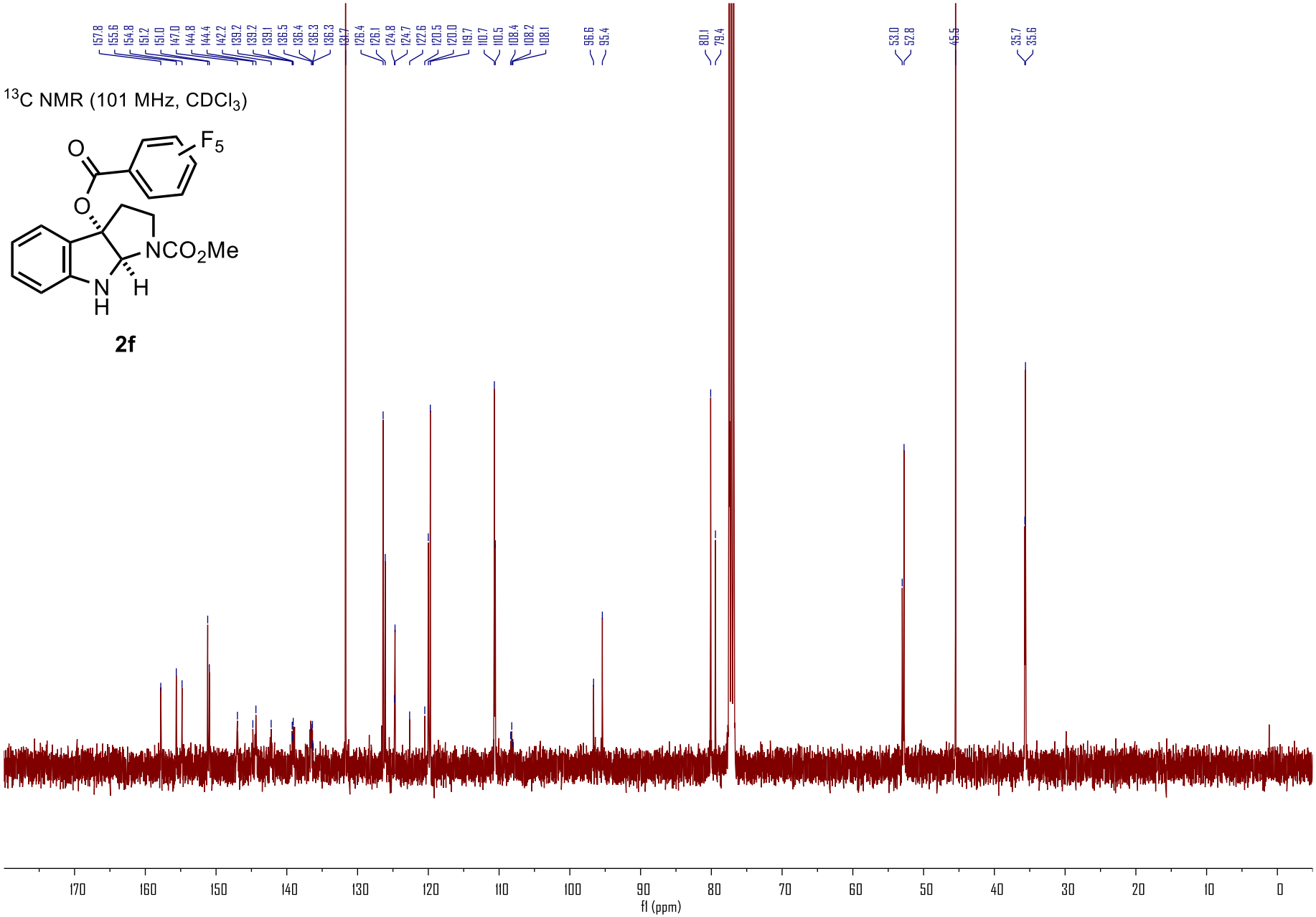


2e

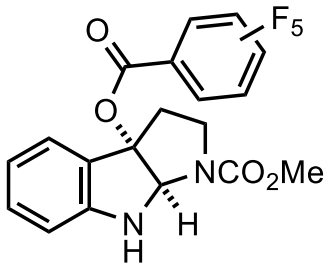
^{1}H NMR (400 MHz, $CDCl_3$)



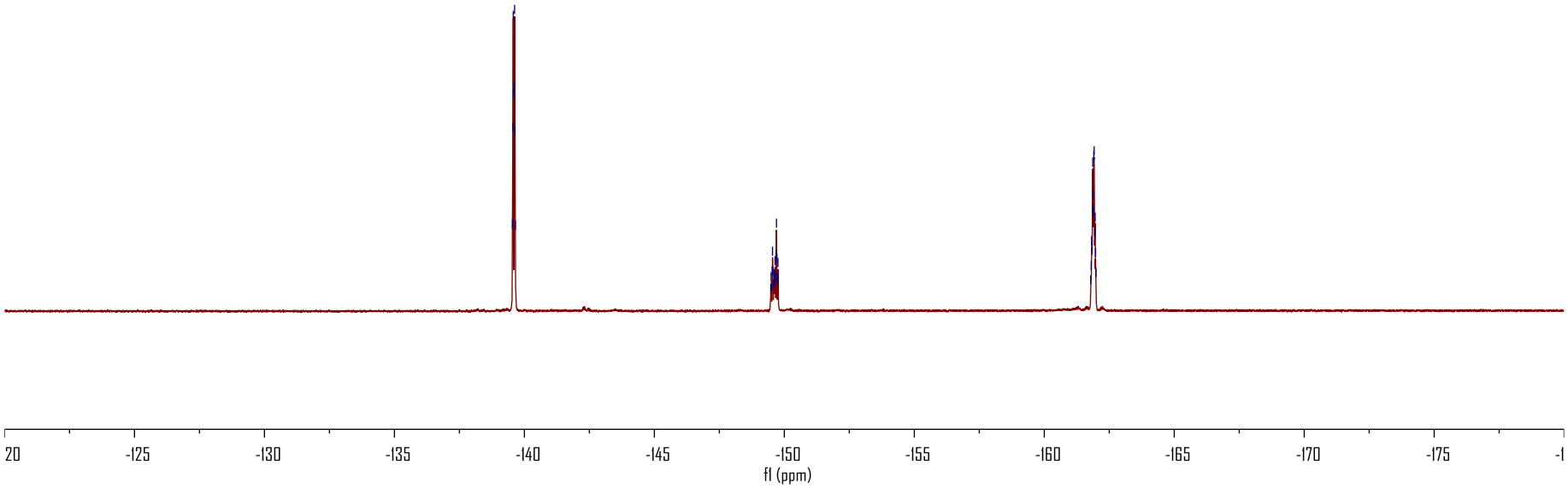
2f

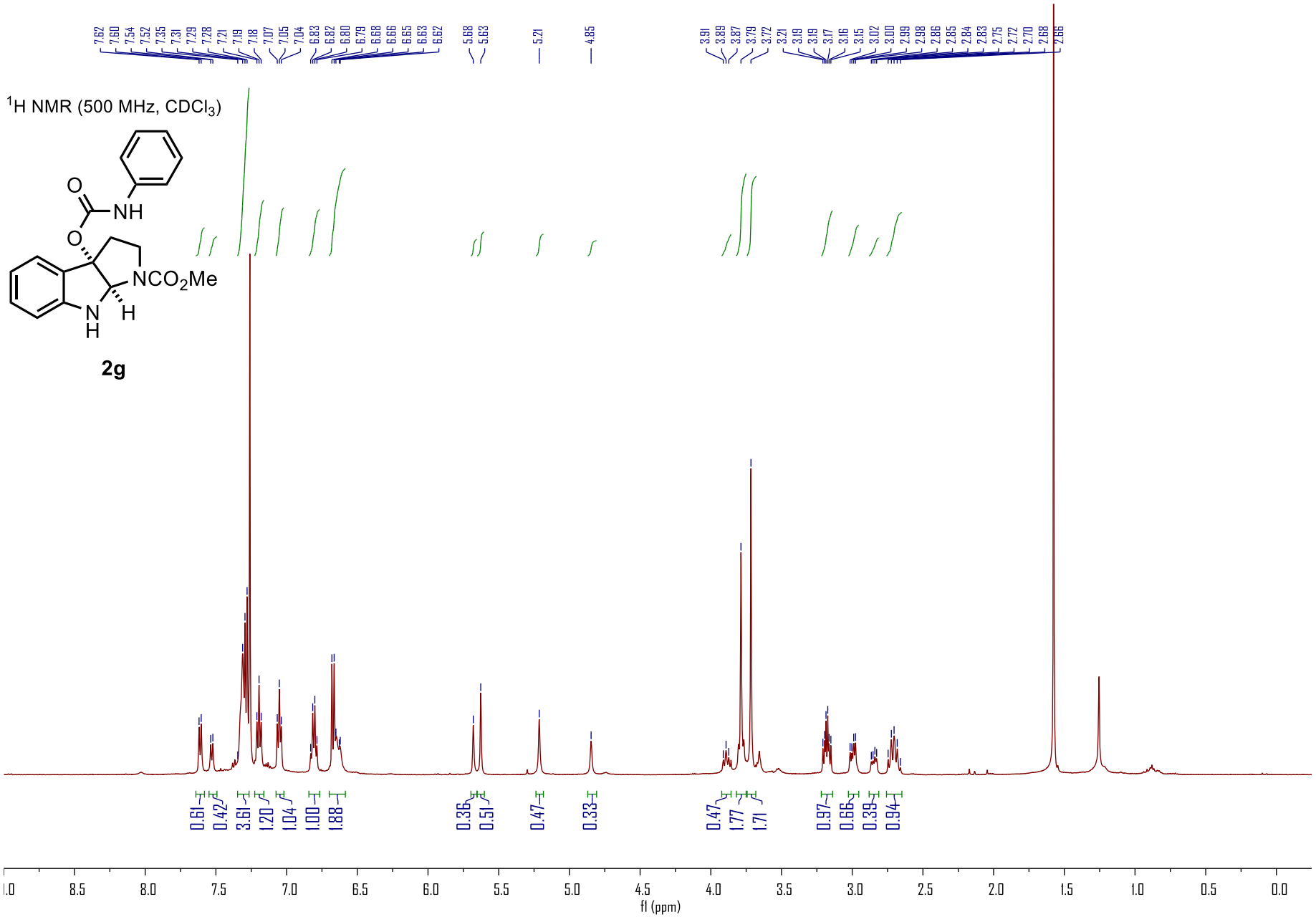

157.8
155.6
154.8
151.2
151.0
147.0
144.8
144.4
142.2
139.2
139.2
139.1
136.5
136.4
136.3
136.3
131.7
128.4
126.1
124.8
124.7
122.6
120.5
120.0
119.7
110.7
110.5
108.4
108.2
108.1
96.6
95.4
80.1
79.4
53.0
52.8
45.5
35.7
35.6
^{13}C NMR (101 MHz, $CDCl_3$)
O
O
F_5
NCO_2Me
N
H
H
2f
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

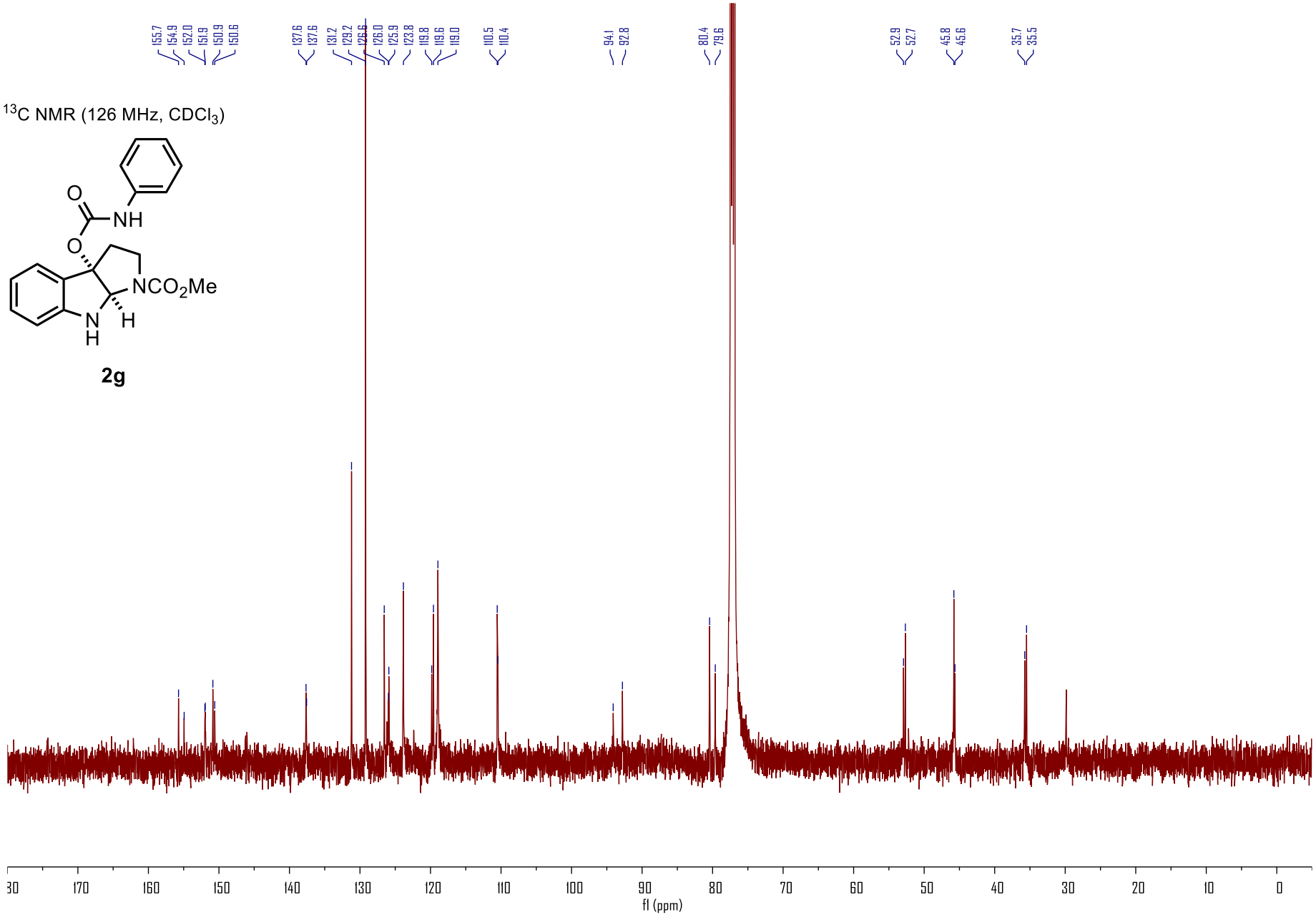
^{19}F NMR (376 MHz, $CDCl_3$)

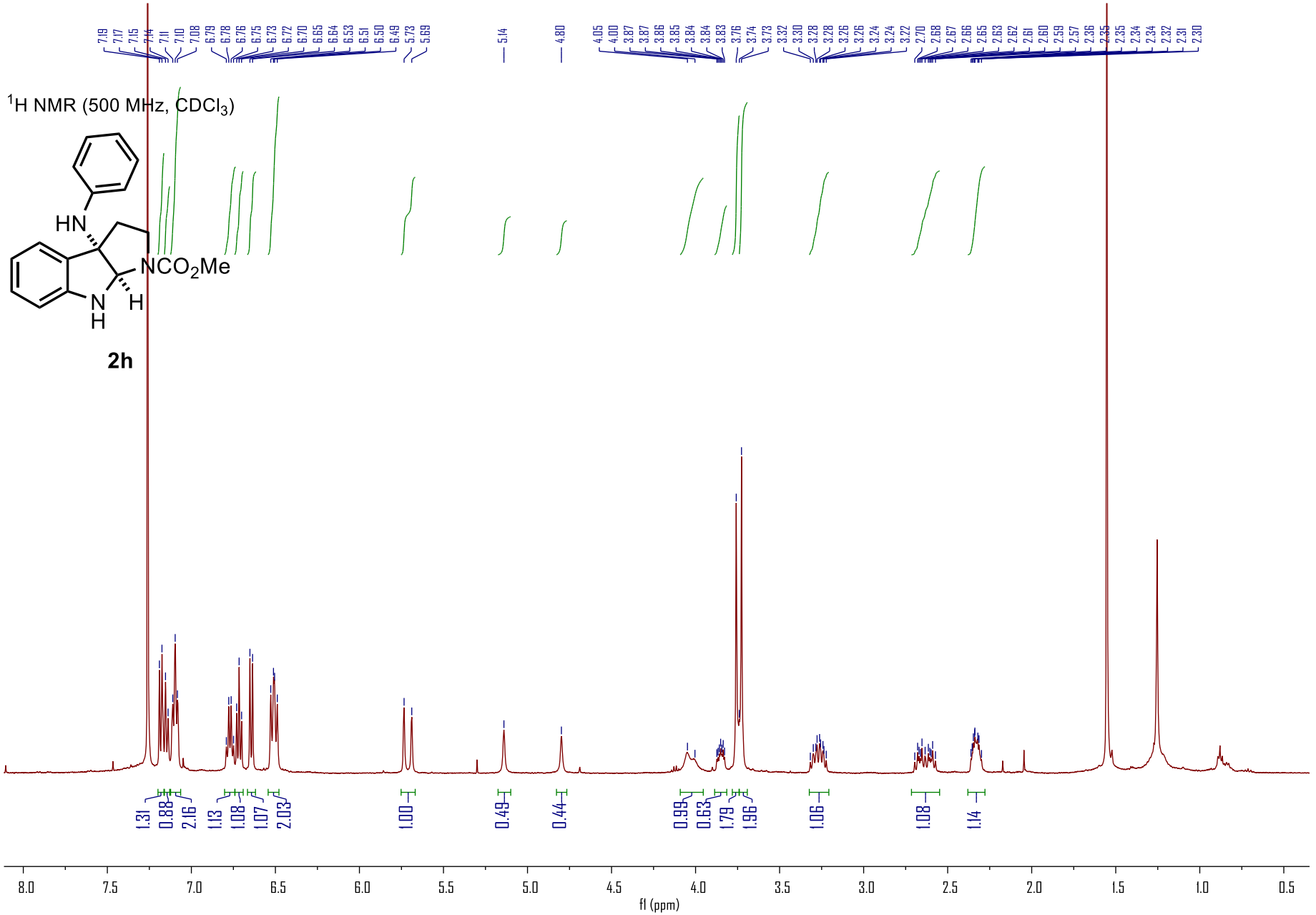


2f

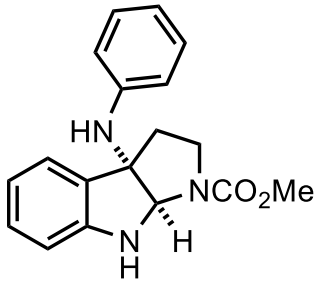



^{1}H NMR (500 MHz, $CDCl_3$)
O
NH
O
NCO_2Me
N
H
H
2g
7.62 7.60 7.54 7.52 7.35 7.31 7.29 7.28 7.21 7.19 7.18 7.07 7.05 7.04 6.83 6.82 6.80 6.79 6.68 6.66 6.65 6.63 6.62
5.68 5.63
5.21
4.85
3.91 3.88 3.87 3.79 3.72 3.21 3.19 3.19 3.17 3.16 3.15 3.02 3.00 2.99 2.98 2.86 2.85 2.84 2.83 2.75 2.72 2.70 2.68 2.66
0.61 0.42 3.61 1.20 1.04 1.00 1.88
0.36 0.51
0.47
0.33
0.47 1.77 1.71
0.97 0.66 0.39 0.94
f1 (ppm)

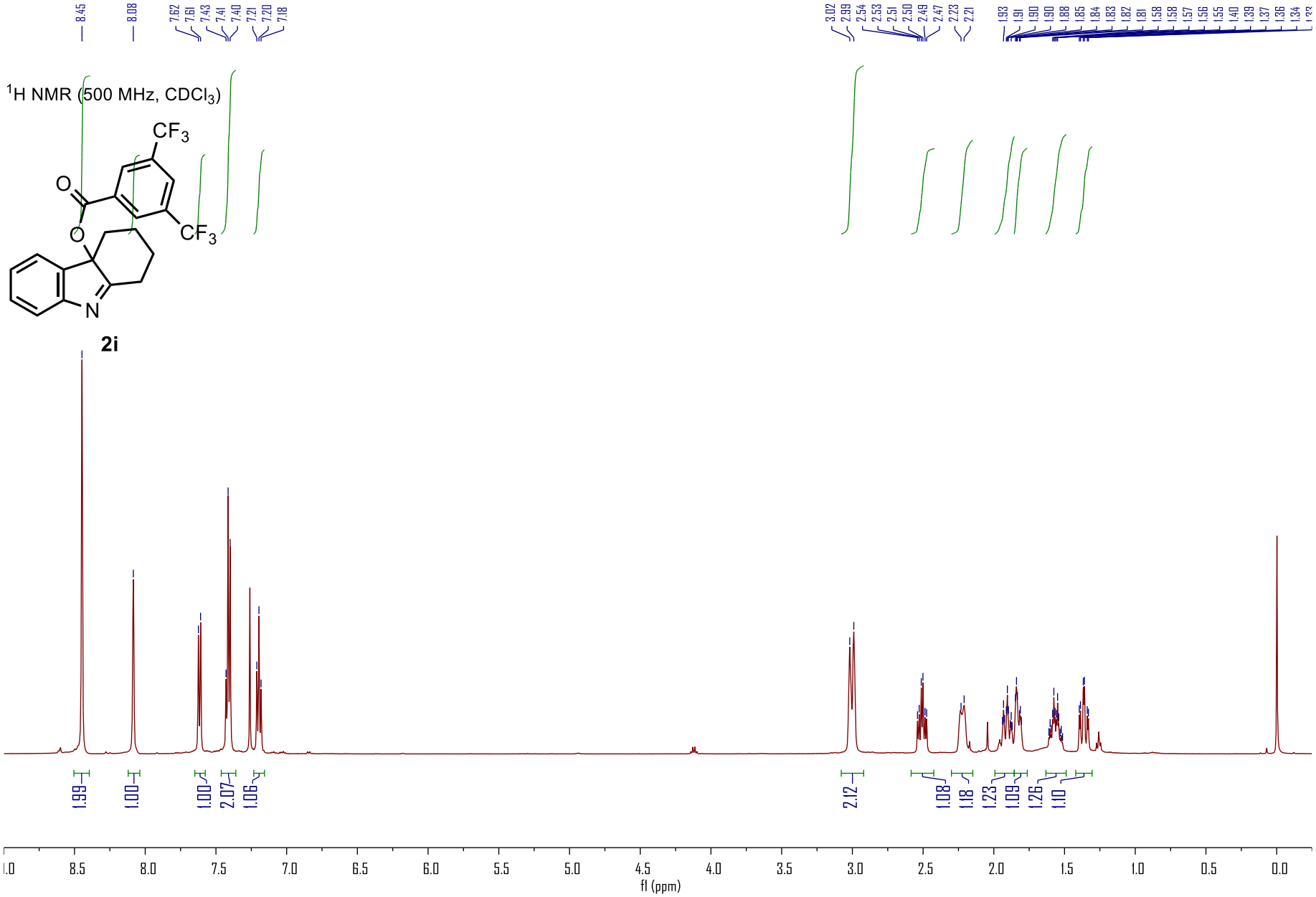

155.7
154.9
152.0
151.9
150.9
150.6
137.6
137.6
131.2
129.2
126.6
126.0
125.9
123.8
119.8
119.6
119.0
110.5
110.4
94.1
92.8
80.4
79.6
52.9
52.7
45.8
45.6
35.7
35.5
^{13}C NMR (126 MHz, $CDCl_3$)
O
NH
O
NCO_2Me
N
H
H
2g
f1 (ppm)

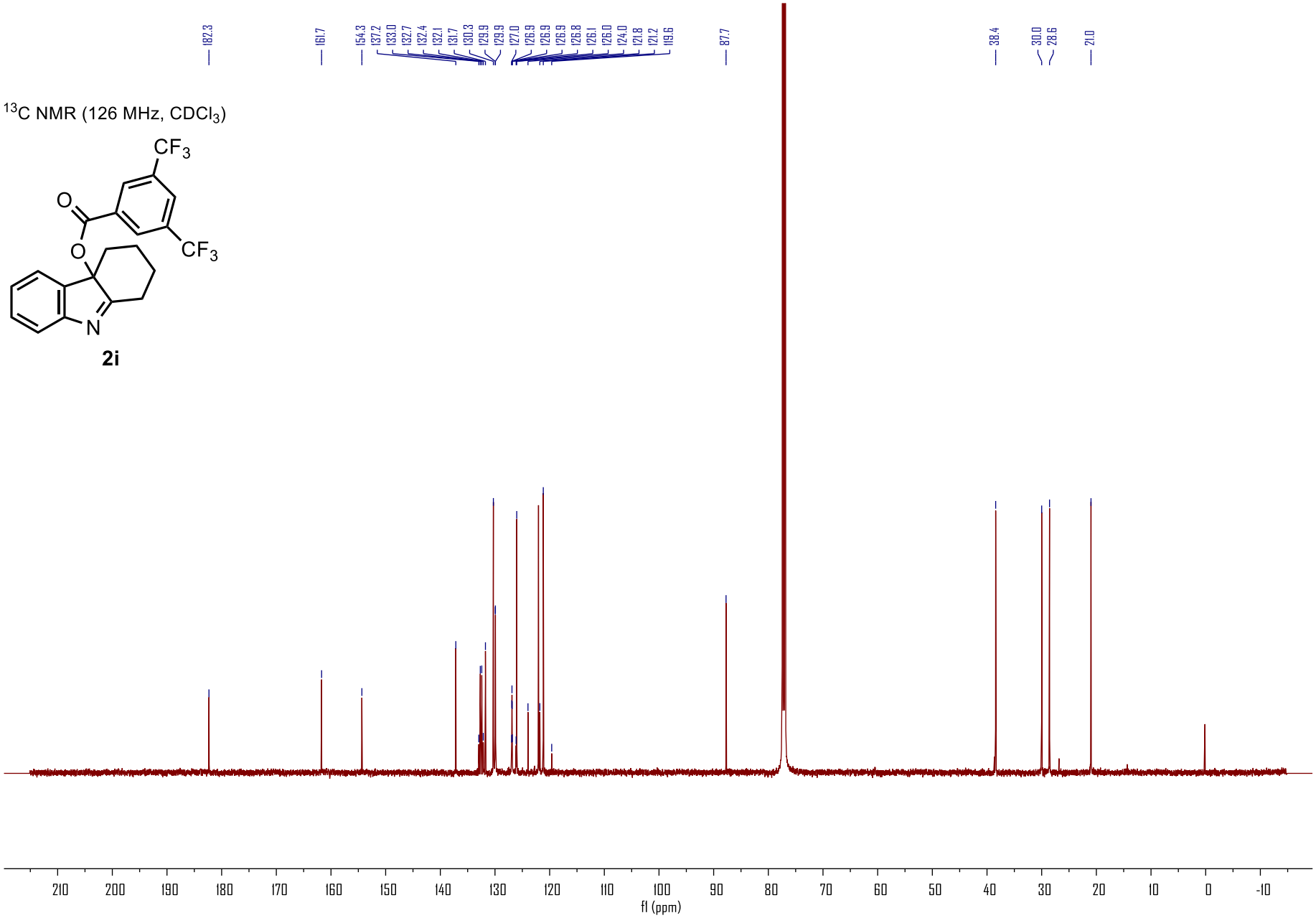

^{1}H NMR (500 MHz, $CDCl_3$)
HN
NCO$_2$Me
N
H
H
2h
7.19 7.17 7.15 7.14 7.11 7.10 7.08 6.79 6.78 6.76 6.75 6.73 6.72 6.70 6.65 6.64 6.53 6.51 6.50 6.49 5.73 5.69 5.14 4.80 4.05 4.00 3.87 3.87 3.86 3.85 3.84 3.84 3.83 3.76 3.74 3.73 3.32 3.30 3.28 3.28 3.26 3.26 3.24 3.24 3.22 2.70 2.68 2.67 2.66 2.65 2.63 2.62 2.61 2.60 2.59 2.57 2.36 2.35 2.35 2.34 2.34 2.32 2.31 2.30
1.31 0.88 2.16 1.13 1.08 1.07 2.03 1.00 0.49 0.44 0.99 0.63 1.79 1.96 1.06 1.08 1.14
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

^{13}C NMR (126 MHz, $CDCl_3$)

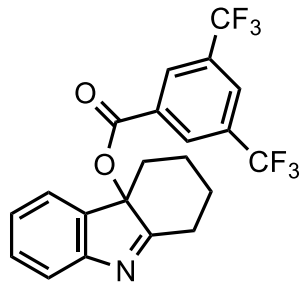


2h

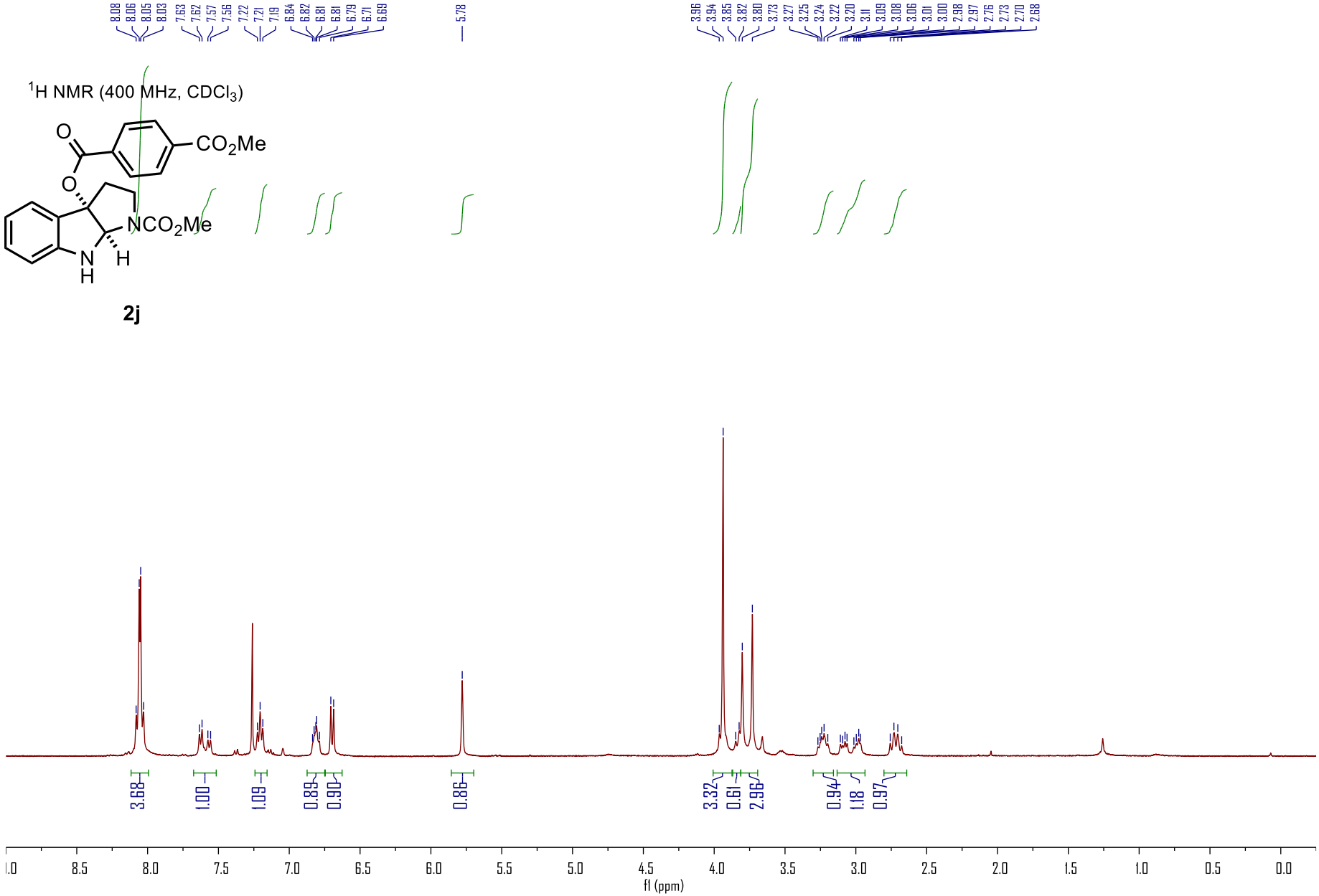

8.45
8.08
7.62
7.61
7.43
7.41
7.40
7.21
7.20
7.18
3.02
2.99
2.54
2.53
2.51
2.50
2.49
2.47
2.23
2.21
1.93
1.91
1.90
1.90
1.88
1.85
1.84
1.83
1.82
1.81
1.58
1.58
1.57
1.56
1.55
1.40
1.39
1.37
1.36
1.34
1H NMR (500 MHz, CDCl3)
CF3
CF3
O
O
N
2i
1.99
1.00
1.00
2.07
1.06
2.12
1.08
1.18
1.23
1.09
1.26
1.10
f1 (ppm)


182.3
161.7
154.3
137.2
133.0
132.7
132.4
132.1
131.7
130.3
129.9
129.9
127.0
126.9
126.9
126.9
126.8
126.1
126.0
124.0
121.8
121.2
119.6
87.7
38.4
30.0
28.6
21.0
^{13}C NMR (126 MHz, $CDCl_3$)
CF_3
CF_3
O
O
N
2i
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

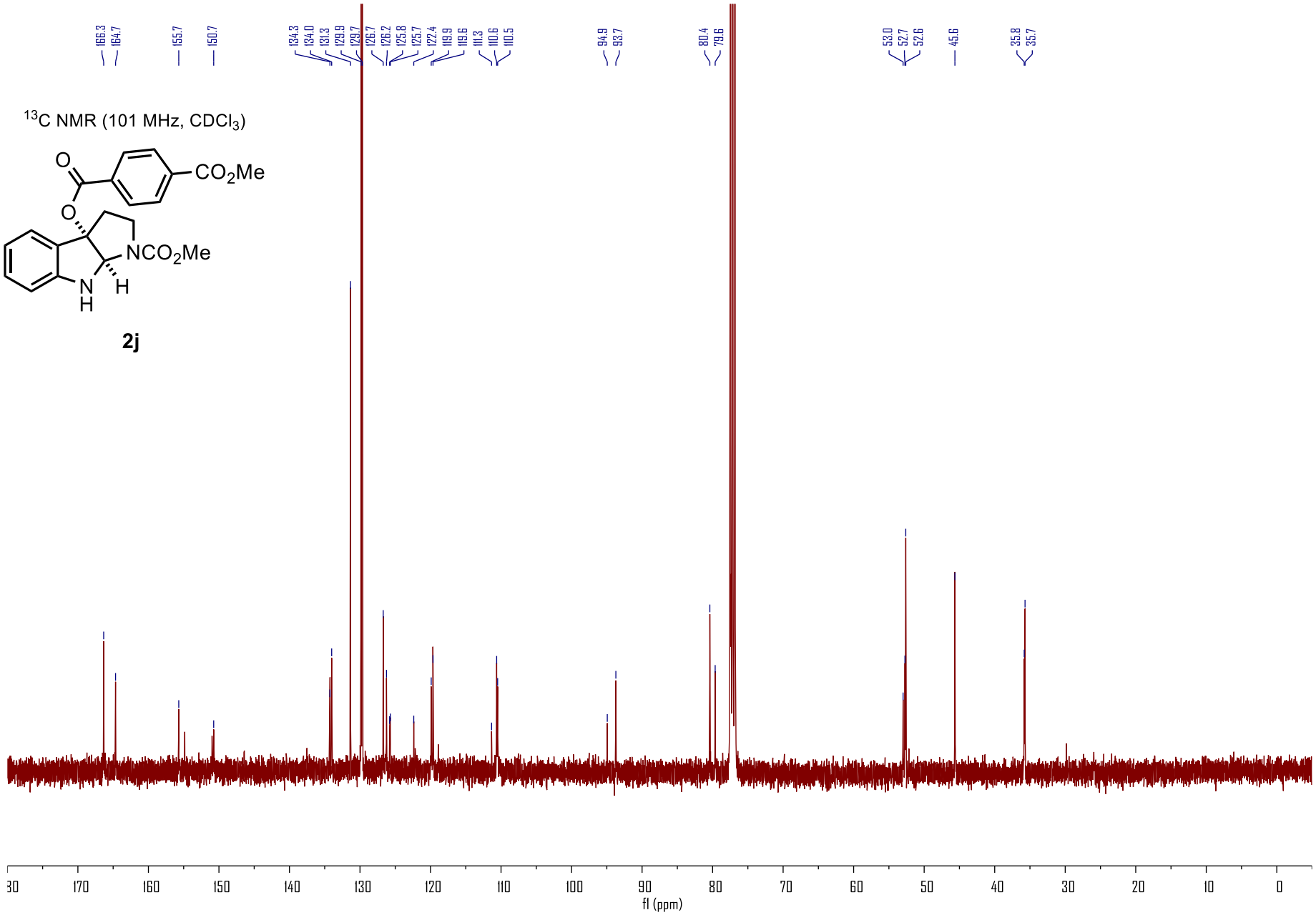
^{19}F NMR (471 MHz, $CDCl_3$)



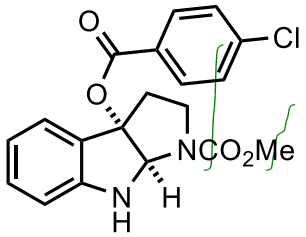
2i


8.08
8.06
8.05
8.03
7.63
7.62
7.57
7.56
7.22
7.21
7.19
6.84
6.82
6.81
6.81
6.79
6.71
6.69
5.78
3.96
3.94
3.85
3.82
3.80
3.73
3.27
3.25
3.24
3.22
3.20
3.11
3.09
3.08
3.06
3.01
3.00
2.98
2.97
2.76
2.73
2.70
2.68
^{1}H NMR (400 MHz, $CDCl_3$)
O
CO_2Me
O
NCO_2Me
N
H
H
3.68
1.00
1.09
0.89
0.90
0.86
3.32
0.61
2.96
0.94
1.18
0.97
f1 (ppm)

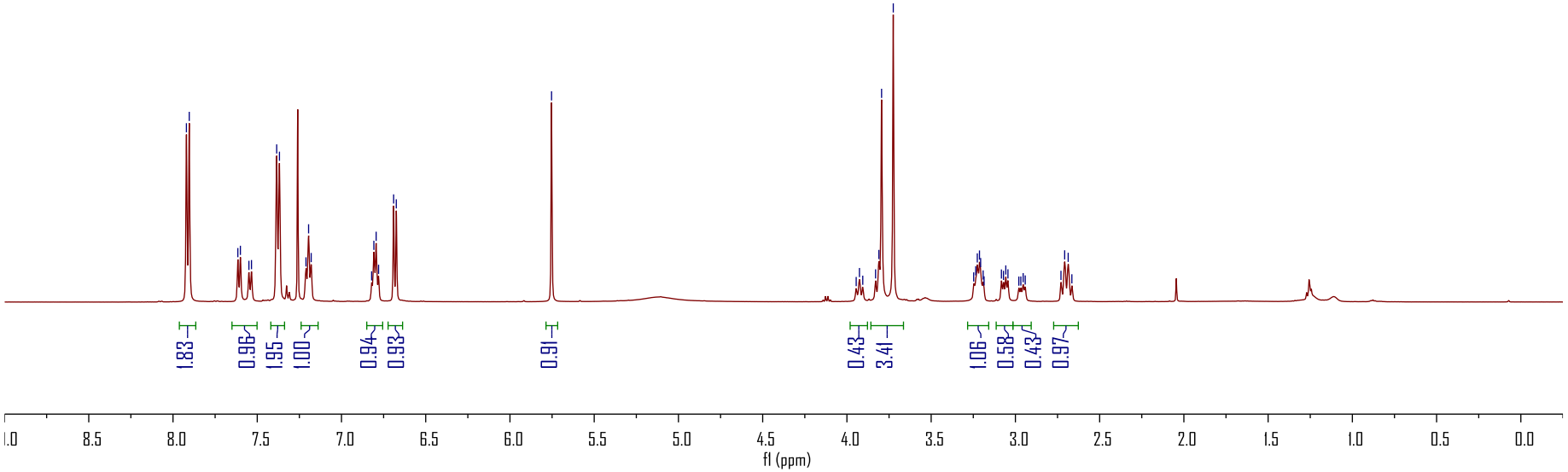
2j

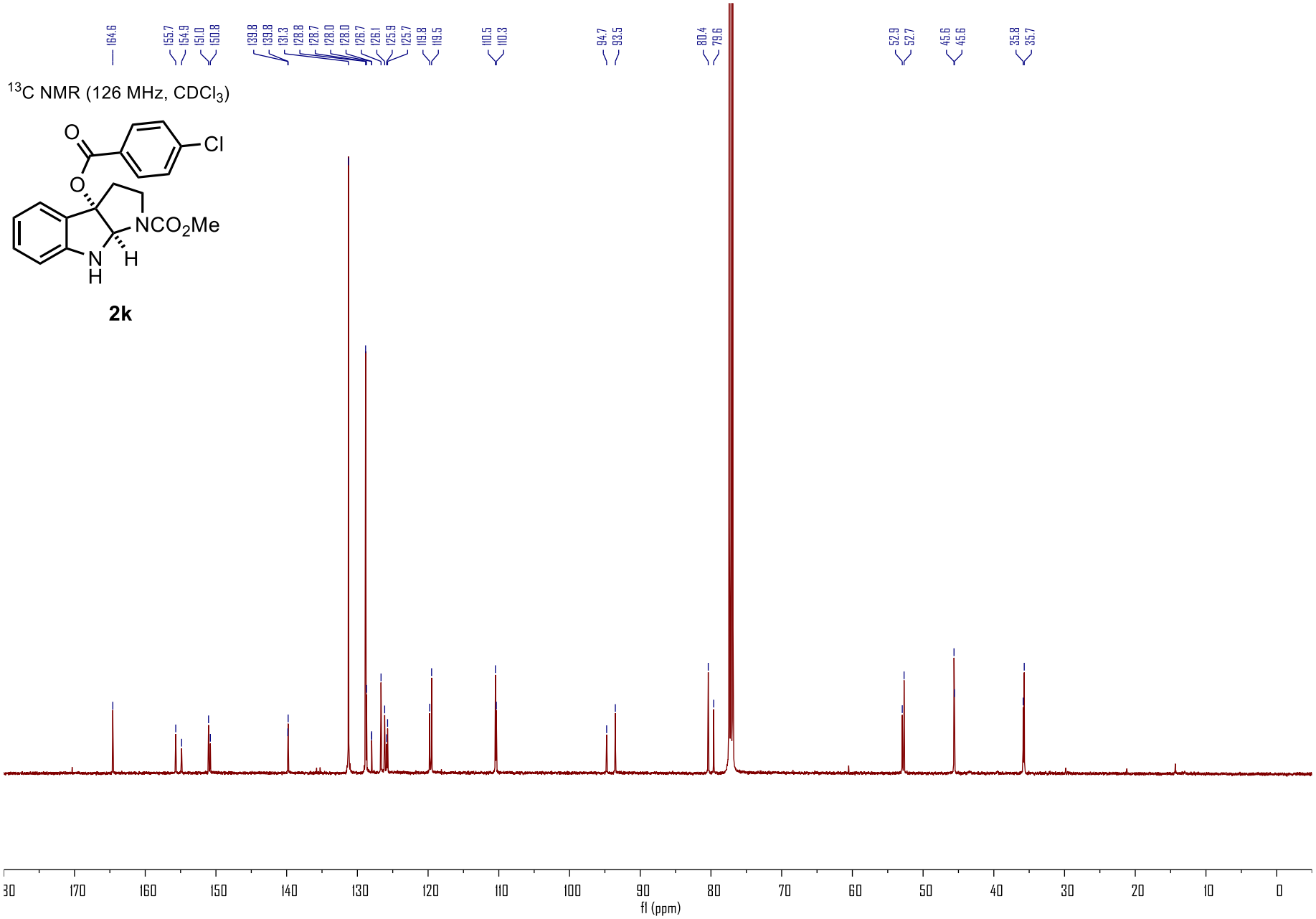

166.3
164.7
155.7
150.7
134.3
134.0
131.3
129.9
129.7
126.7
126.2
125.8
125.7
122.4
119.9
119.6
111.3
110.6
110.5
94.9
93.7
80.4
79.6
53.0
52.7
52.6
45.6
35.8
35.7
^{13}C NMR (101 MHz, $CDCl_3$)
O
CO_2Me
O
NCO_2Me
N
H
H
2j
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

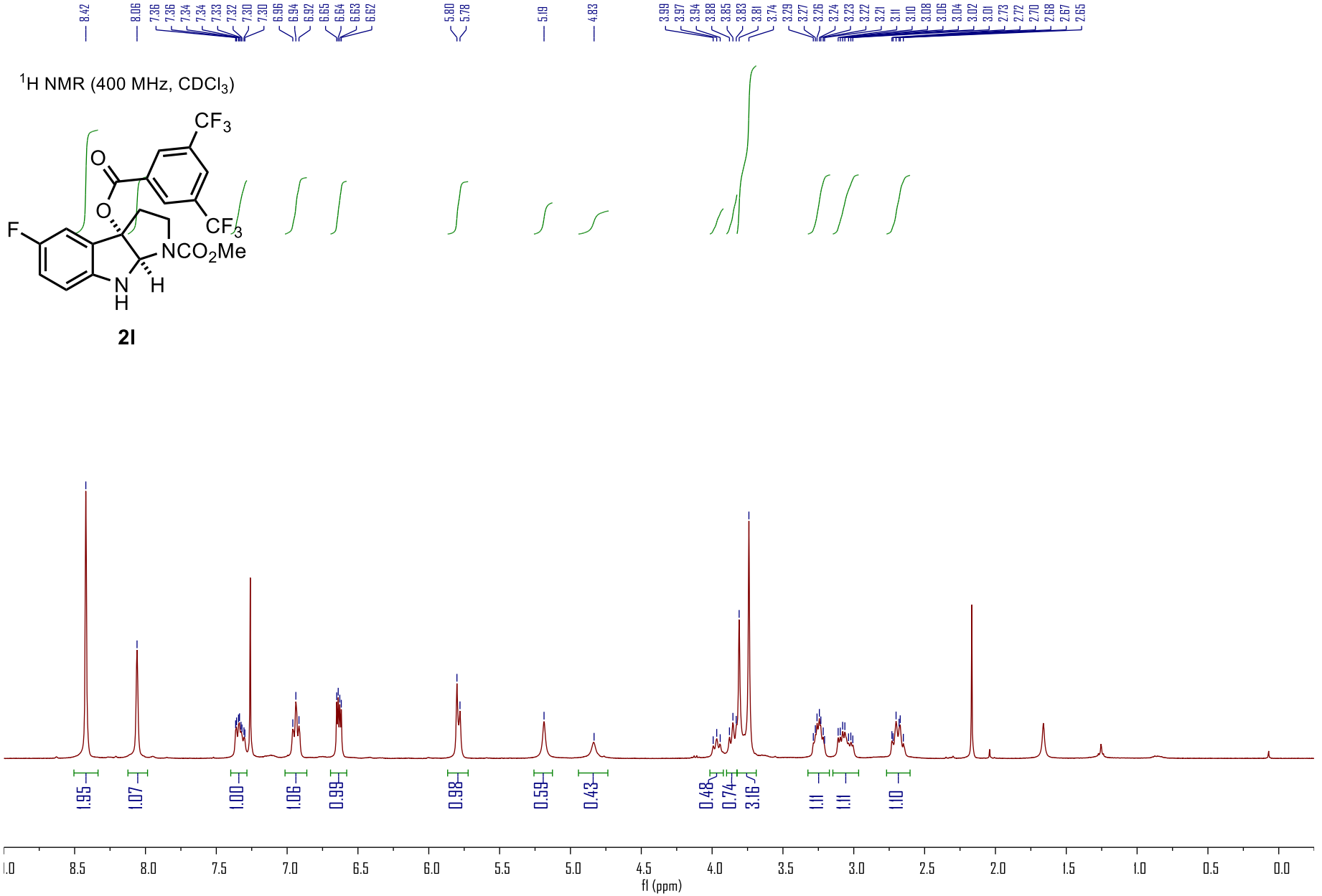
^{1}H NMR (500 MHz, $CDCl_3$)

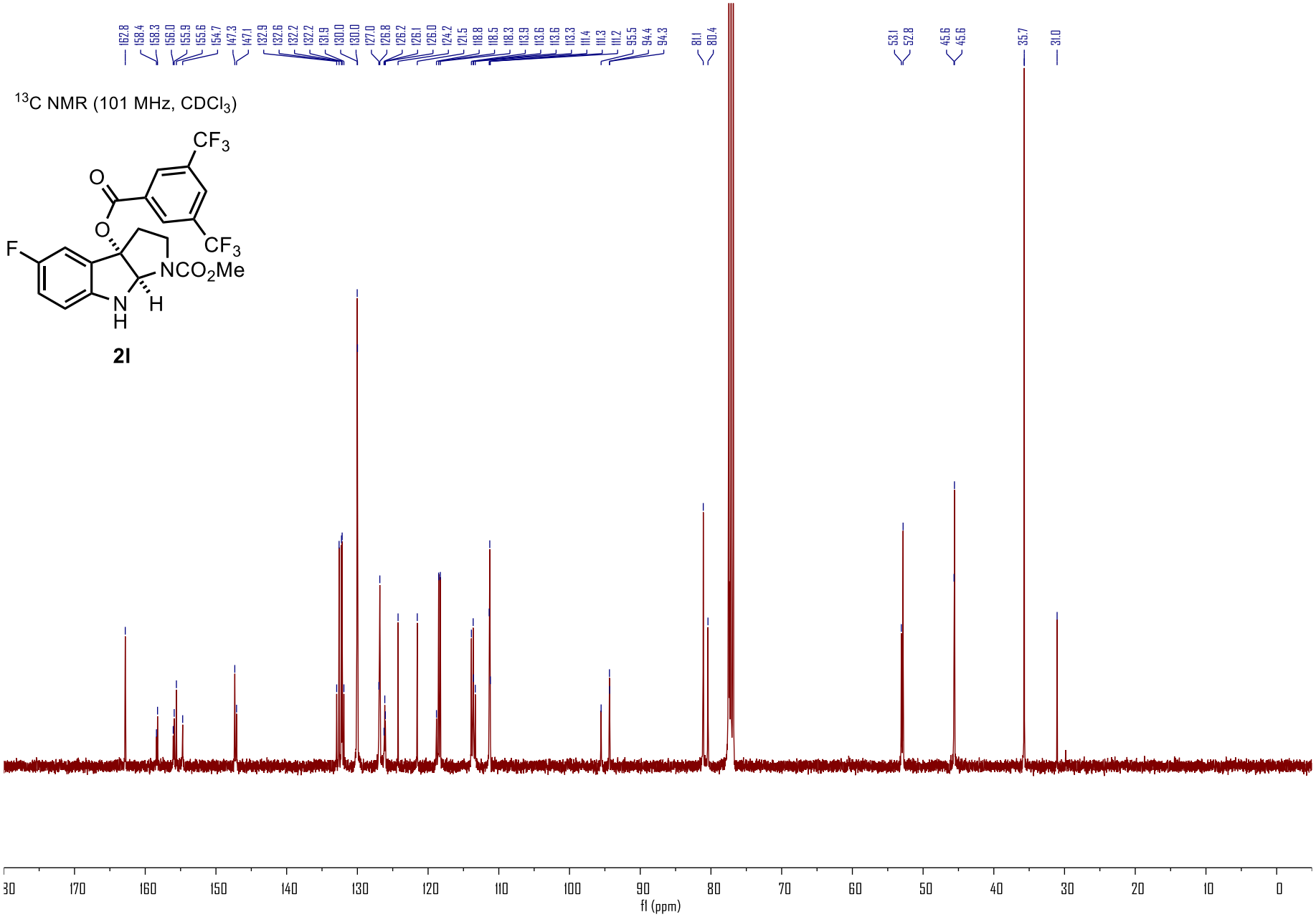


2k

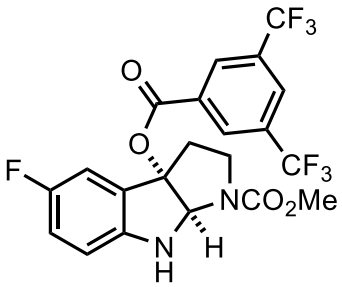



164.6
155.7
154.9
151.0
150.8
139.8
139.8
131.3
128.8
128.7
128.0
128.0
126.7
126.1
125.9
125.7
119.8
119.5
110.5
110.3
94.7
93.5
80.4
79.6
52.9
52.7
45.6
45.6
35.8
35.7
13C NMR (126 MHz, CDCl3)
O
Cl
O
NCO2Me
N
H
H
2k
f1 (ppm)

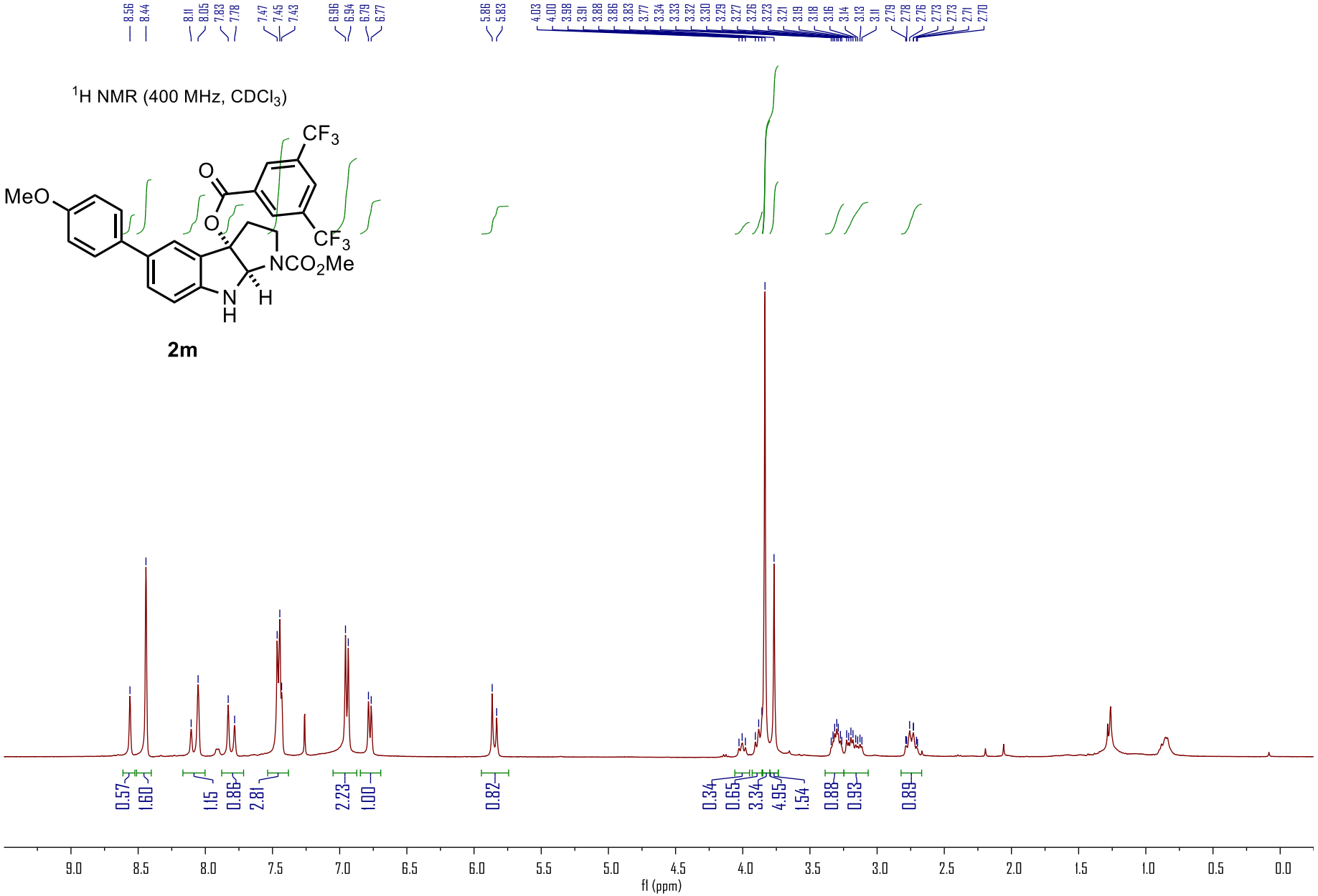

8.42
8.06
7.36
7.36
7.34
7.34
7.33
7.32
7.30
7.30
6.96
6.94
6.92
6.65
6.64
6.63
6.62
5.80
5.78
5.19
4.83
3.99
3.97
3.94
3.88
3.85
3.83
3.81
3.74
3.29
3.27
3.26
3.24
3.23
3.22
3.21
3.11
3.10
3.08
3.06
3.04
3.02
3.01
2.73
2.72
2.70
2.68
2.67
2.65
1H NMR (400 MHz, CDCl3)
CF3
O
O
CF3
F
NCO2Me
N
H
H
2I
1.95
1.07
1.00
1.06
0.99
0.98
0.59
0.43
0.48
0.74
3.16
1.11
1.11
1.10
f1 (ppm)

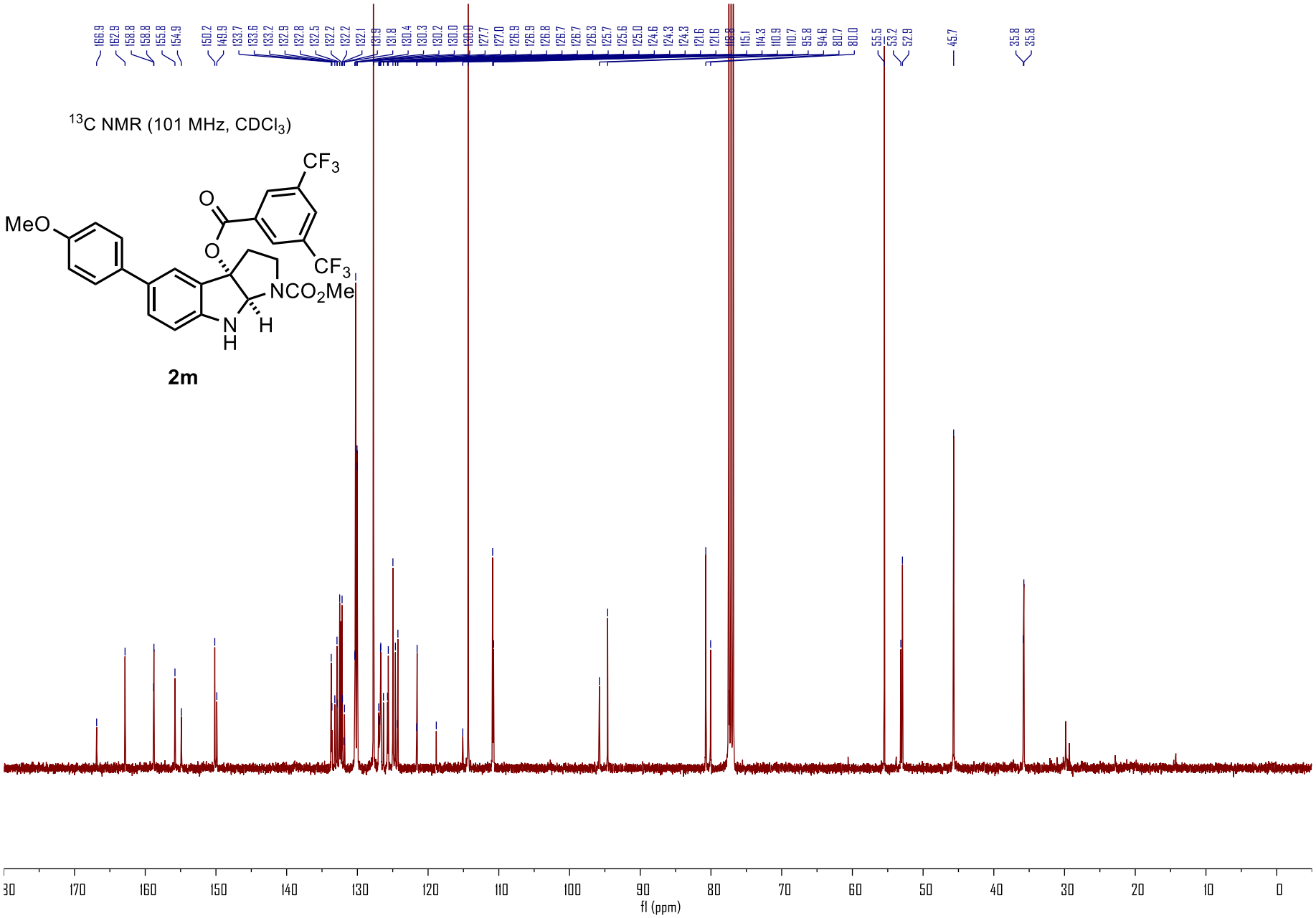

162.8
158.4
158.3
156.0
155.9
155.6
154.7
147.3
147.1
132.9
132.6
132.2
132.2
131.9
130.0
130.0
127.0
126.8
126.2
126.1
126.0
124.2
121.5
118.8
118.5
118.3
113.9
113.6
113.6
113.3
111.4
111.3
111.2
95.5
94.4
94.3
81.1
80.4
53.1
52.8
45.6
45.6
35.7
31.0
^{13}C NMR (101 MHz, $CDCl_3$)
CF_3
O
O
CF_3
F
NCO_2Me
N
H
H
2l
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)

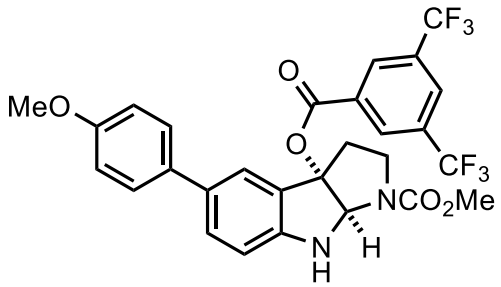


2l


8.56
8.44
8.11
8.05
7.83
7.78
7.47
7.45
7.43
6.96
6.94
6.79
6.77
5.86
5.83
4.03
4.00
3.98
3.91
3.88
3.86
3.83
3.77
3.34
3.33
3.32
3.30
3.29
3.27
3.26
3.23
3.21
3.19
3.18
3.16
3.14
3.13
3.11
2.79
2.78
2.76
2.73
2.73
2.71
2.70
^{1}H NMR (400 MHz, $CDCl_3$)
MeO
O
O
CF_3
CF_3
NCO_2Me
N
H
H
2m
0.57
1.60
1.15
0.86
2.81
2.23
1.00
0.82
0.34
0.65
3.34
4.95
1.54
0.88
0.93
0.89
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

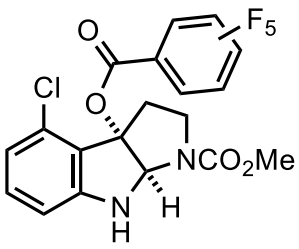

166.9
162.9
158.8
158.8
155.8
154.9
150.2
149.9
133.7
133.6
133.2
132.9
132.8
132.5
132.2
132.2
132.1
131.9
131.8
130.4
130.3
130.2
130.0
128.0
127.7
127.0
126.9
126.9
126.8
126.7
126.7
126.3
125.7
125.6
125.0
124.6
124.3
124.3
121.6
121.6
115.1
114.3
110.9
110.7
95.8
94.6
80.7
80.0
55.5
53.2
52.9
45.7
35.8
35.8
^{13}C NMR (101 MHz, CDCl$_3$)
CF$_3$
O
MeO
O
CF$_3$
NCO$_2$Me
N
H
H
2m
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)

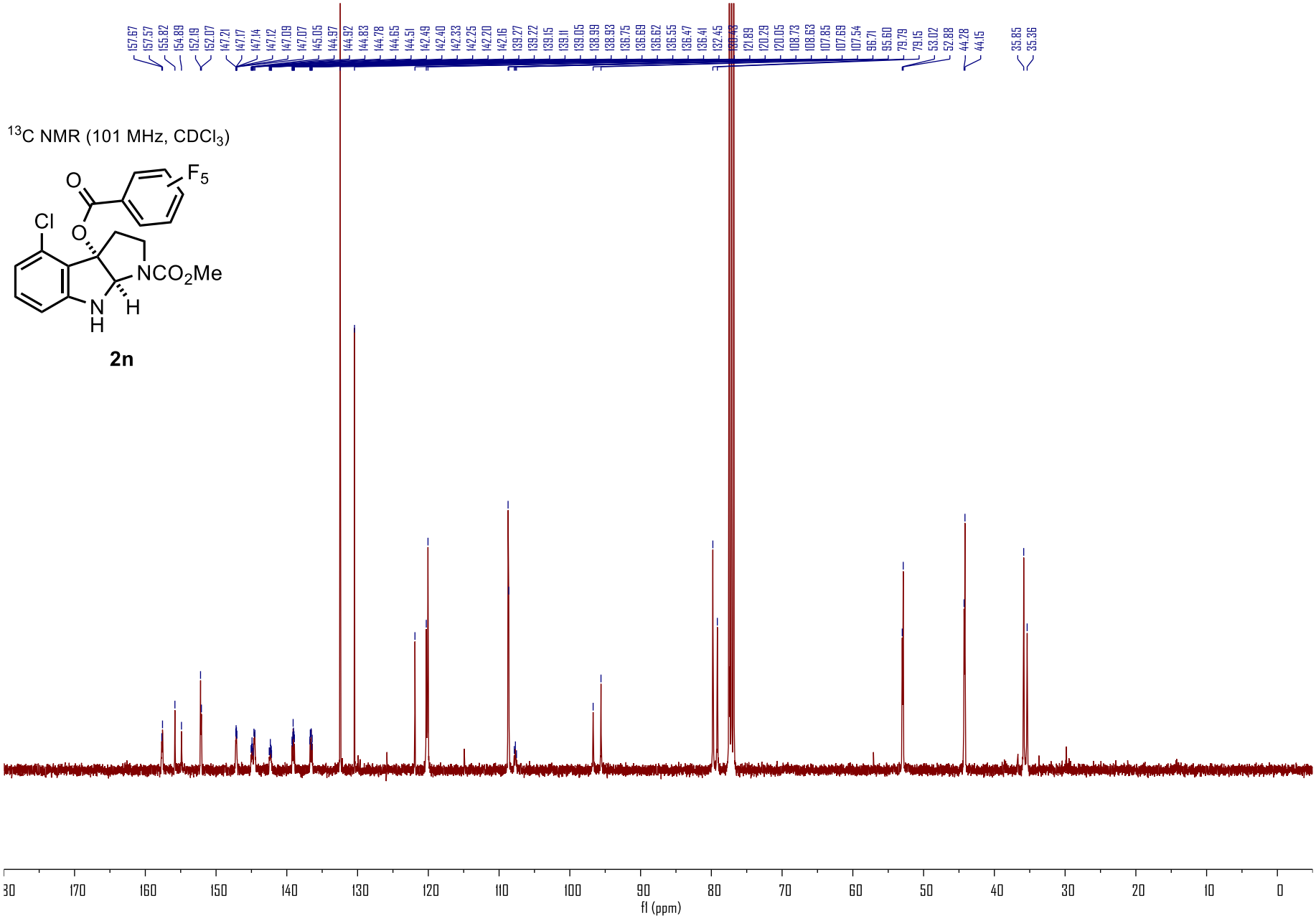


2m

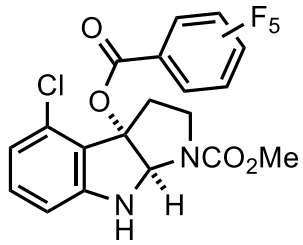
^{1}H NMR (400 MHz, $CDCl_3$)



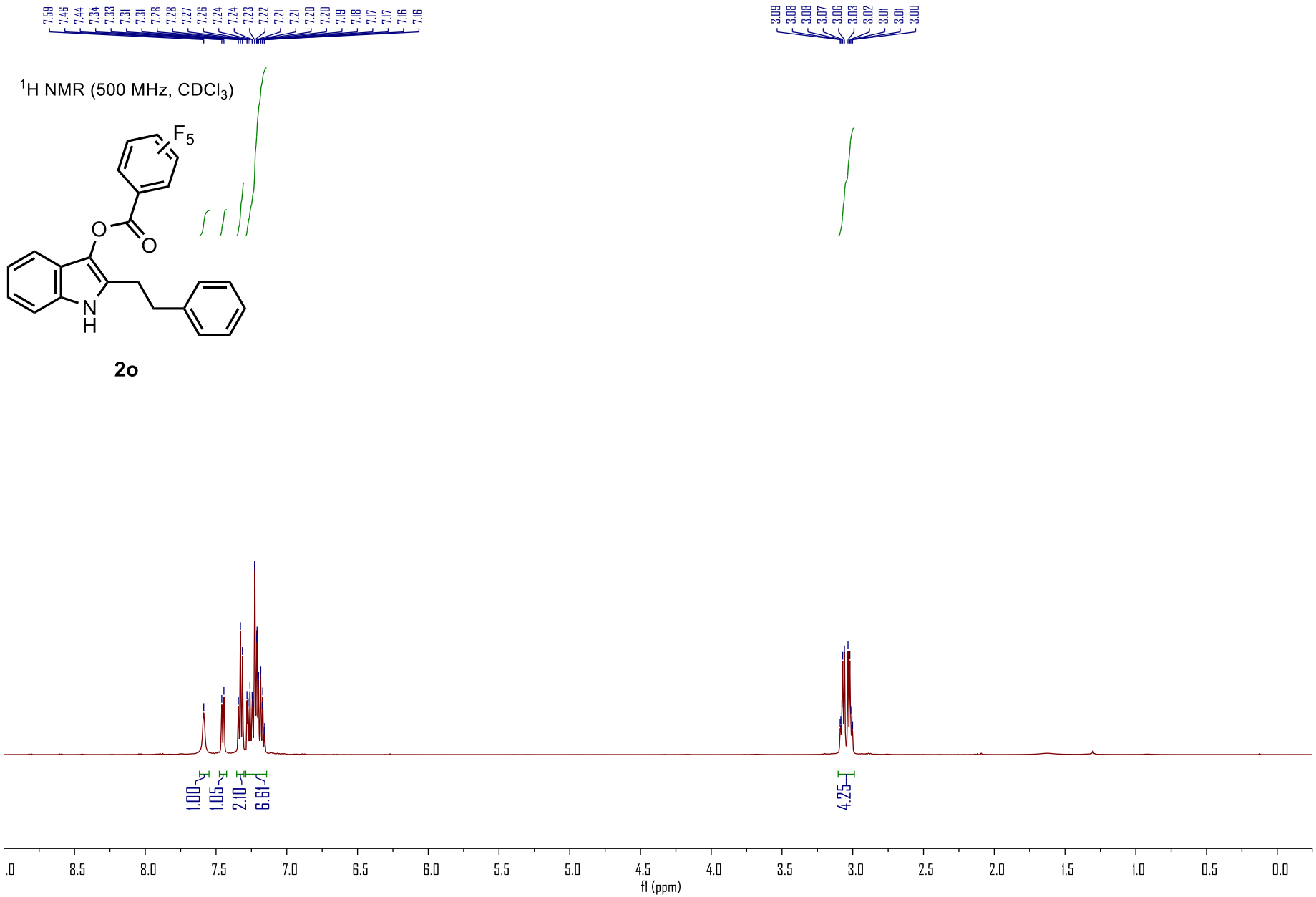
2n

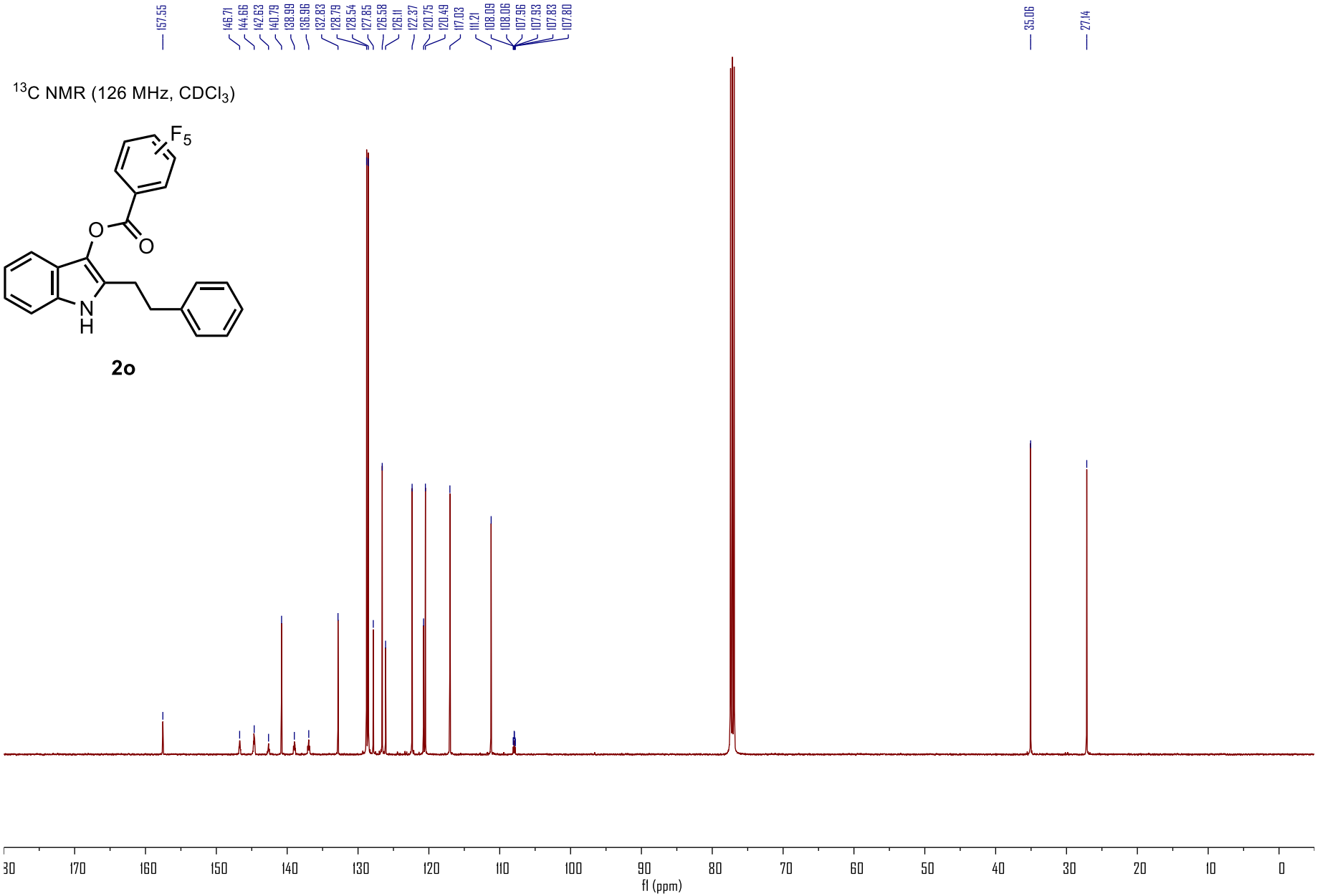

157.67
157.57
155.82
154.88
152.19
152.07
147.21
147.17
147.14
147.12
147.09
147.07
145.05
144.97
144.92
144.83
144.78
144.65
144.51
142.49
142.40
142.33
142.25
142.20
142.16
139.27
139.22
139.15
139.11
139.05
138.99
138.93
136.75
136.69
136.62
136.55
136.47
136.41
132.45
121.89
120.29
120.05
108.73
108.63
107.85
107.69
107.54
96.71
95.60
79.79
79.15
53.02
52.88
44.28
44.15
35.85
35.38
^{13}C NMR (101 MHz, $CDCl_3$)
O
F_5
Cl
O
NCO_2Me
N
H
H
2n
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)

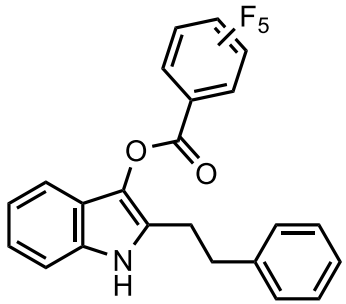


2n

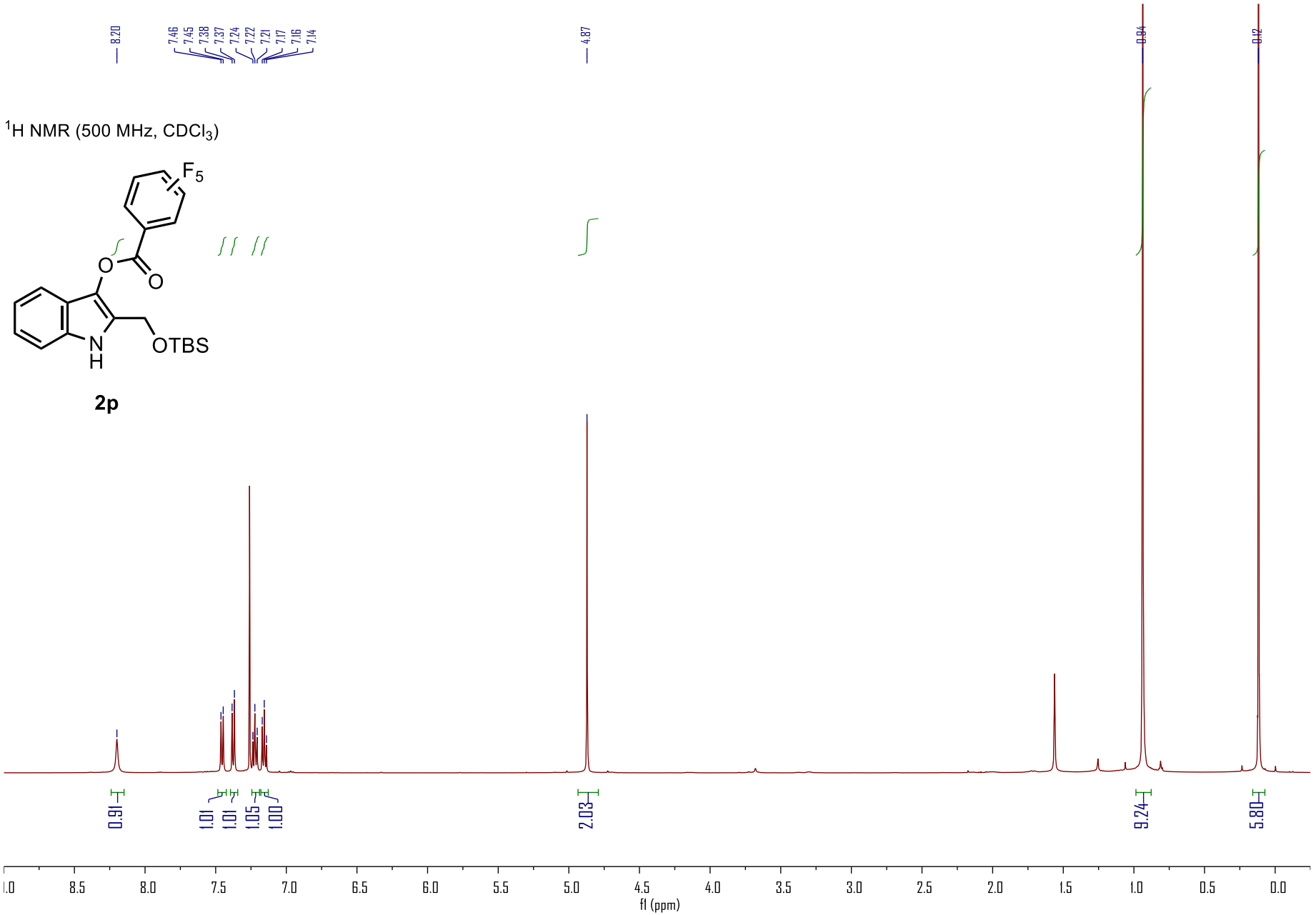

7.59
7.46
7.44
7.34
7.33
7.31
7.31
7.28
7.28
7.27
7.26
7.24
7.24
7.23
7.22
7.21
7.21
7.20
7.20
7.19
7.18
7.17
7.17
7.16
7.16
3.09
3.08
3.08
3.07
3.06
3.03
3.02
3.01
3.01
3.00
^{1}H NMR (500 MHz, $CDCl_3$)
F_5
O
O
N
H
2o
1.00
1.05
2.10
6.61
4.25
f1 (ppm)

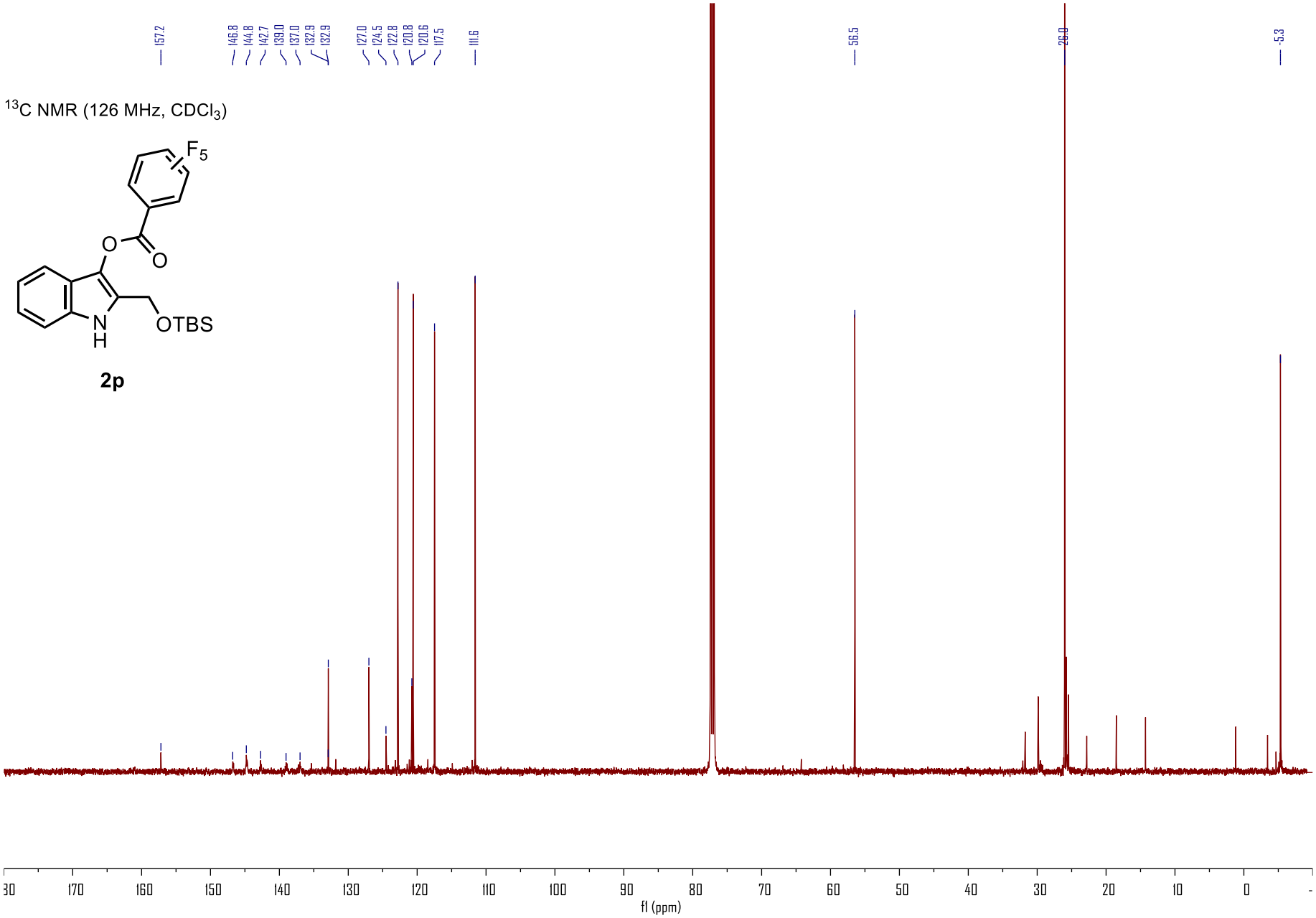

157.55
146.71
144.66
142.63
140.79
138.99
136.96
132.83
128.79
128.54
127.85
126.58
126.11
122.37
120.75
120.49
117.03
111.21
108.09
108.06
107.96
107.93
107.83
107.80
35.06
27.14
13C NMR (126 MHz, CDCl3)
F5
O
O
N
H
2o
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

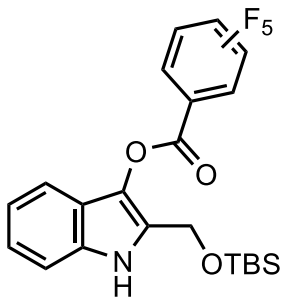


2o


8.20
7.46
7.45
7.38
7.37
7.24
7.22
7.21
7.17
7.16
7.14
4.87
0.94
0.12
^{1}H NMR (500 MHz, $CDCl_3$)
F_5
O
O
N
H
OTBS
2p
0.91
1.01
1.01
1.05
1.00
2.03
9.24
5.80
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

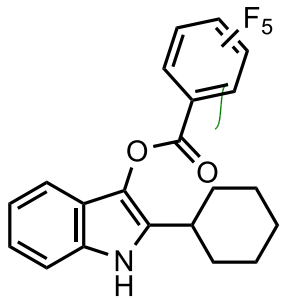

157.2
146.8
144.8
142.7
139.0
137.0
132.9
132.9
127.0
124.5
122.8
120.8
120.6
117.5
111.6
56.5
26.0
-5.3
^{13}C NMR (126 MHz, $CDCl_3$)
F_5
O
O
N
H
OTBS
2p
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

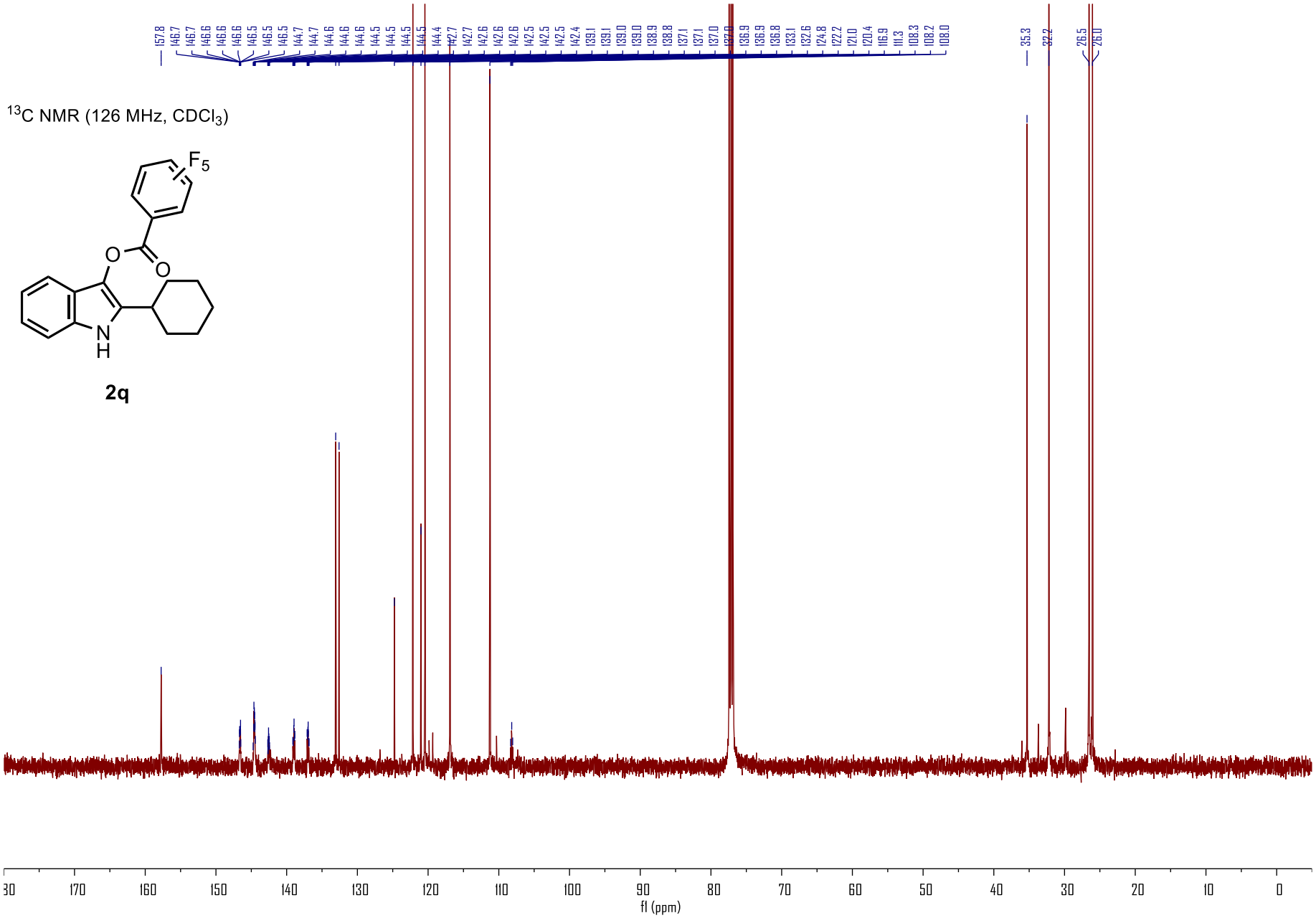


2p

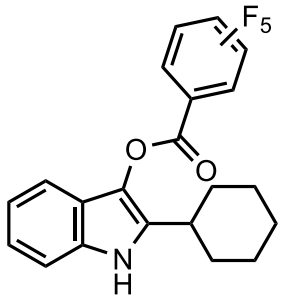
^{1}H NMR (400 MHz, $CDCl_3$)



2q

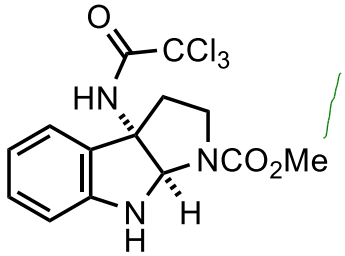

157.8
146.7
146.7
146.6
146.6
146.6
146.5
146.5
146.5
144.7
144.7
144.6
144.6
144.6
144.5
144.5
144.5
144.4
142.7
142.7
142.6
142.6
142.6
142.5
142.5
142.5
142.4
139.1
139.1
139.0
139.0
138.9
138.8
137.1
137.0
136.9
136.9
136.8
133.1
132.6
124.8
122.2
121.0
120.4
116.9
111.3
108.3
108.2
108.0
35.3
32.2
26.5
26.0
13C NMR (126 MHz, CDCl3)
F5
O
O
N
H
2q
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)

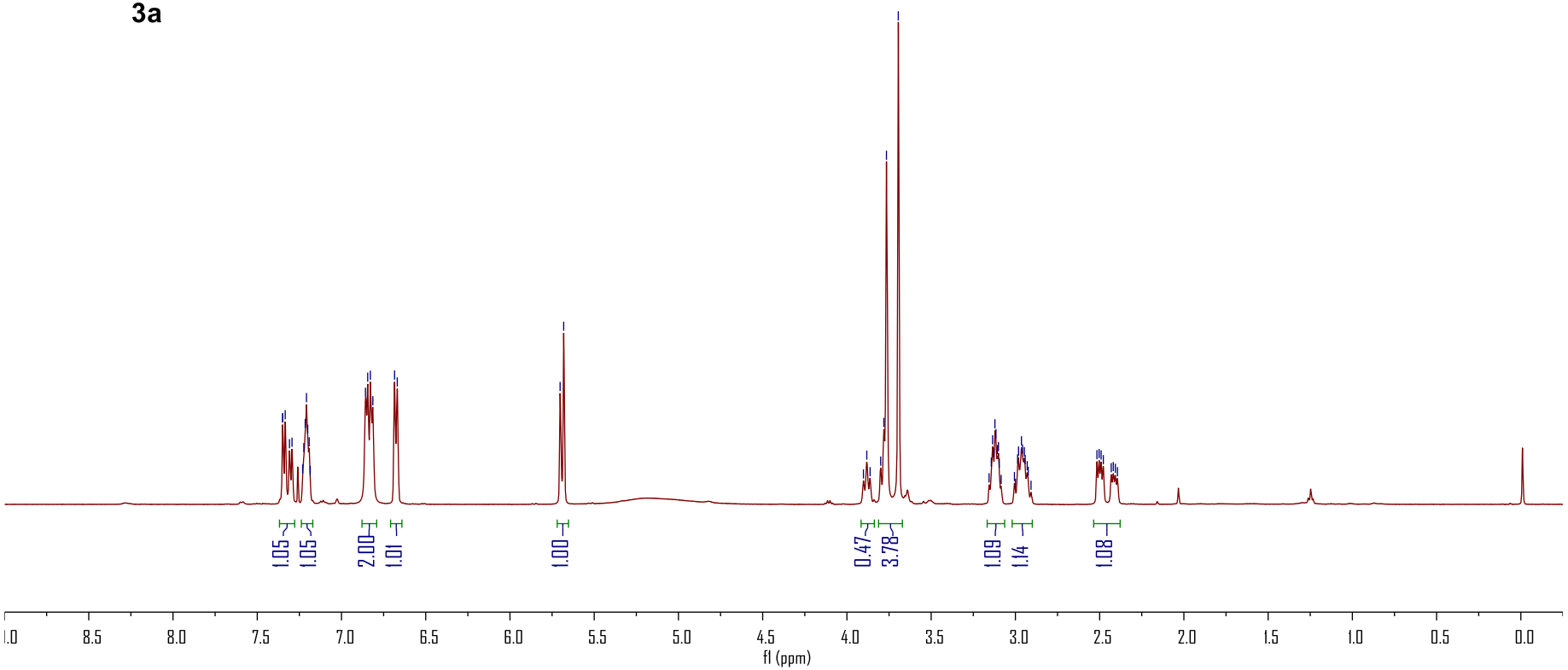


2q

^{1}H NMR (500 MHz, $CDCl_3$)

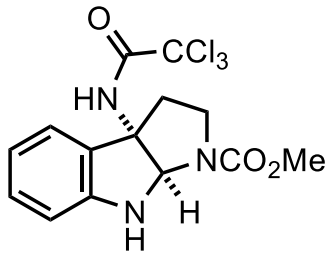


3a

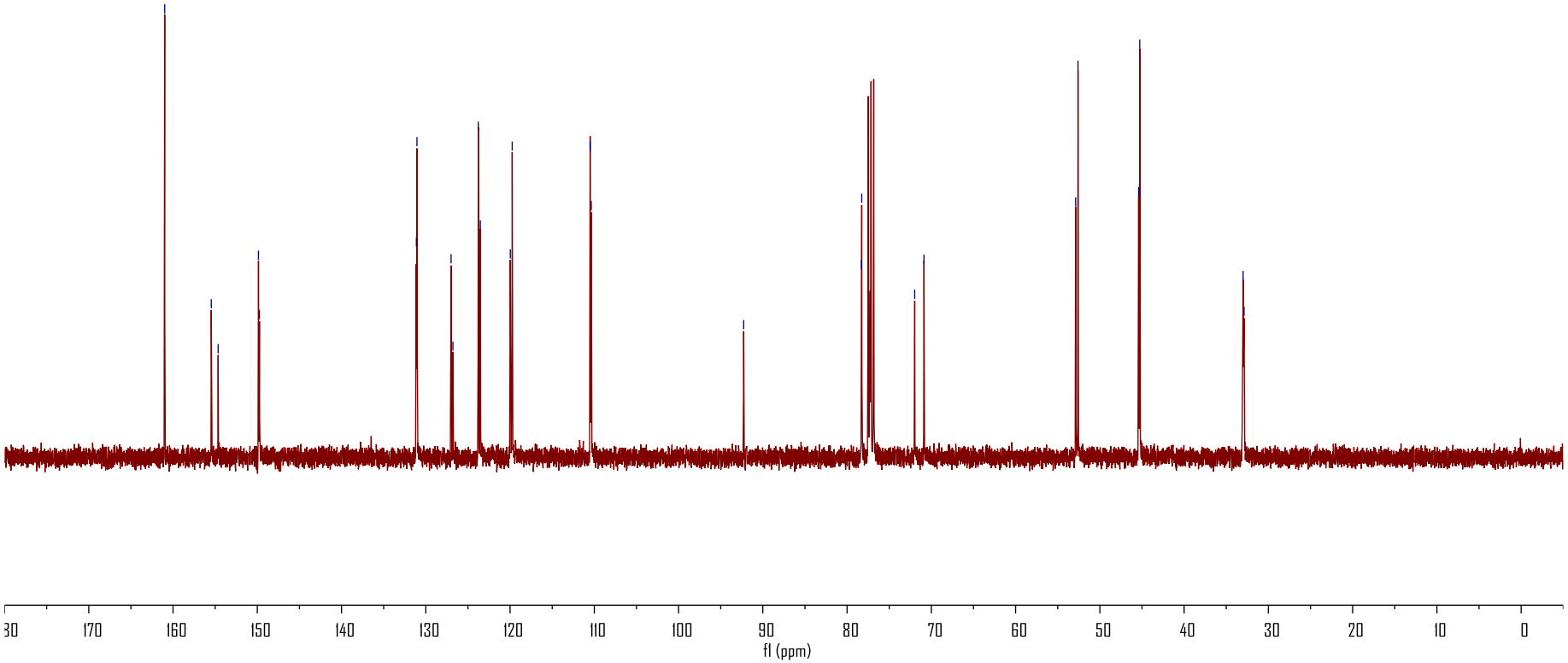


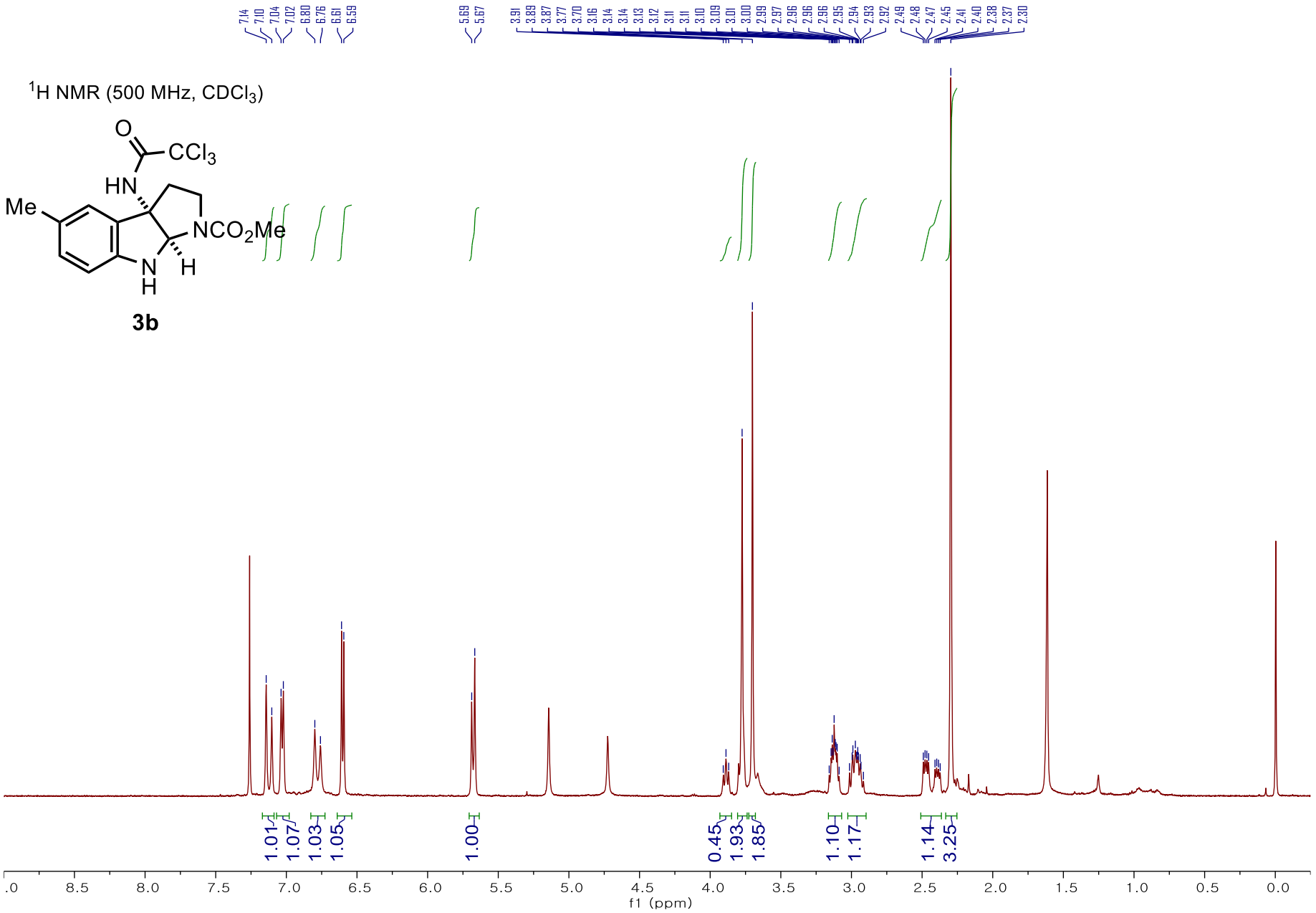
161.0
155.5
154.6
149.9
149.7
131.1
131.1
127.0
126.8
123.8
123.5
120.0
119.7
110.5
110.4
92.3
78.3
78.3
72.0
70.9
52.9
52.6
45.4
45.3
33.0
32.9

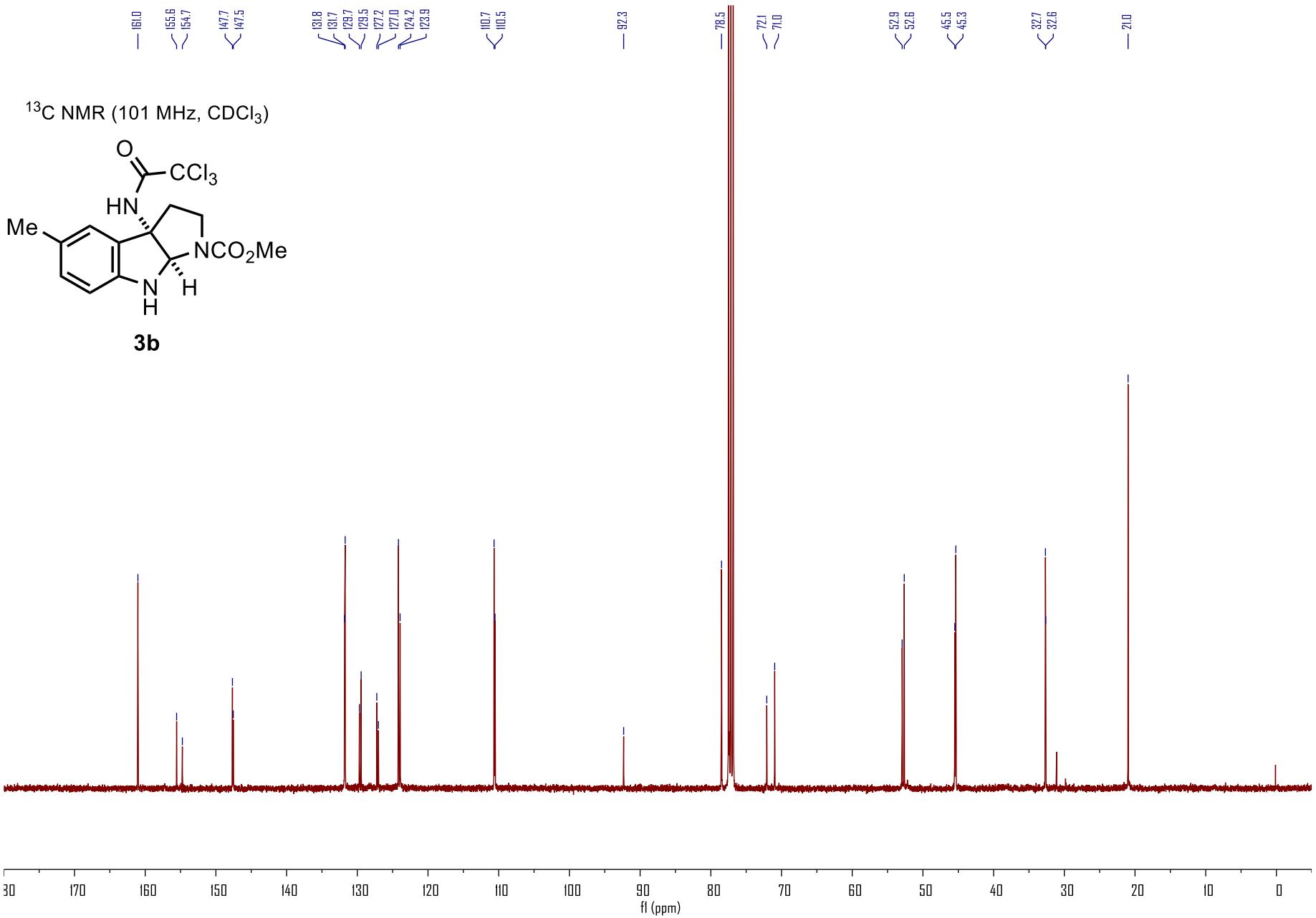
^{13}C NMR (101 MHz, $CDCl_3$)

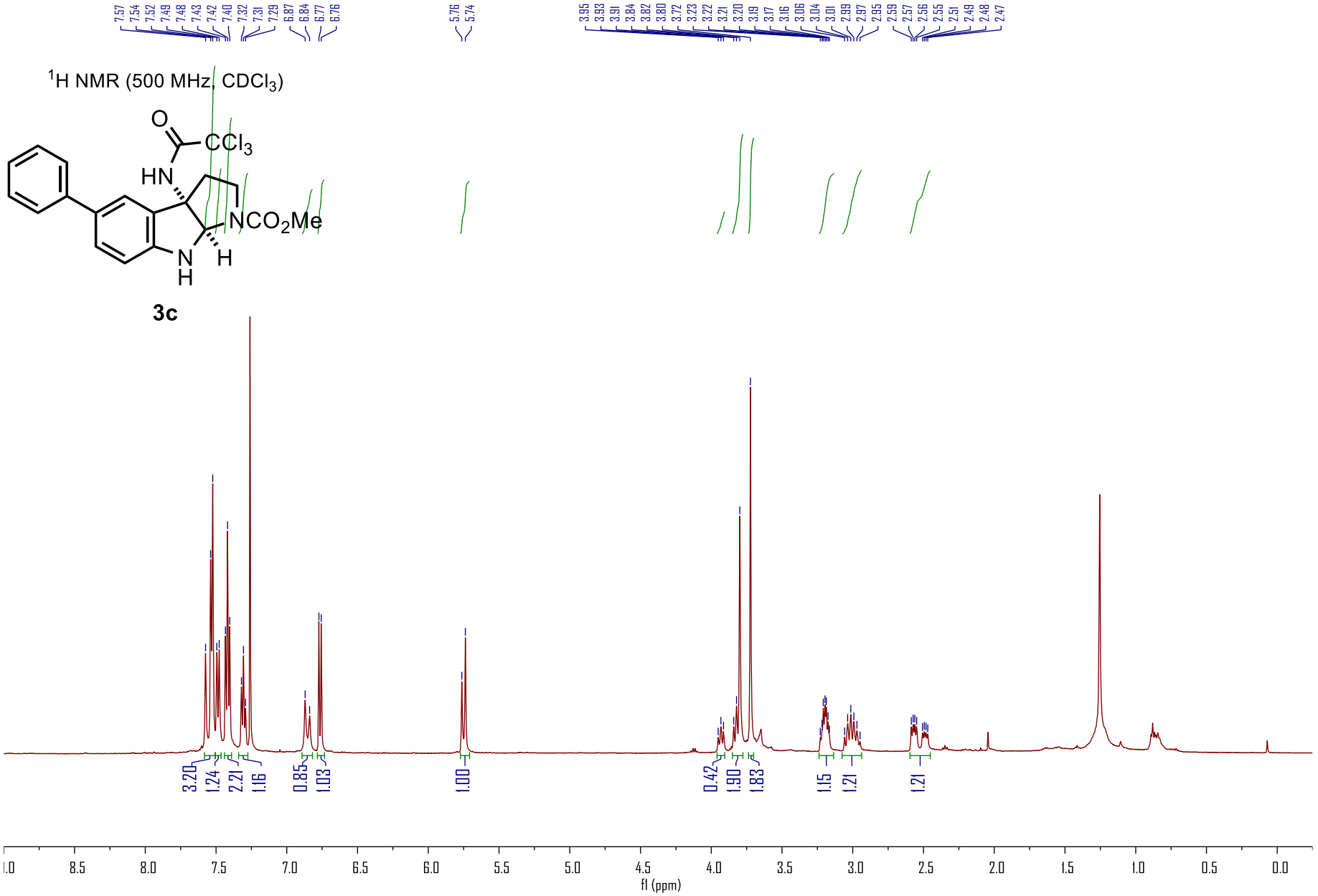


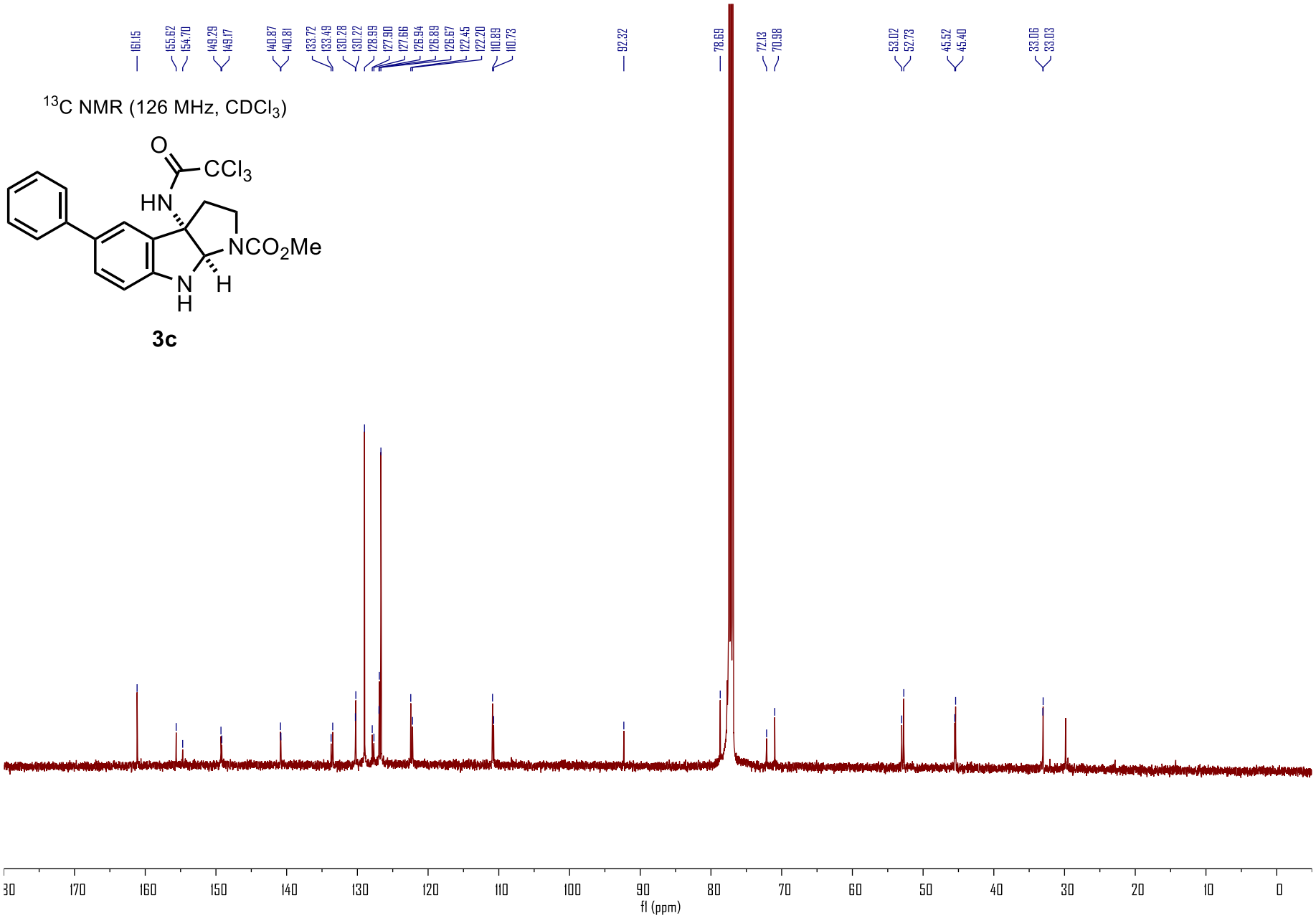
3a

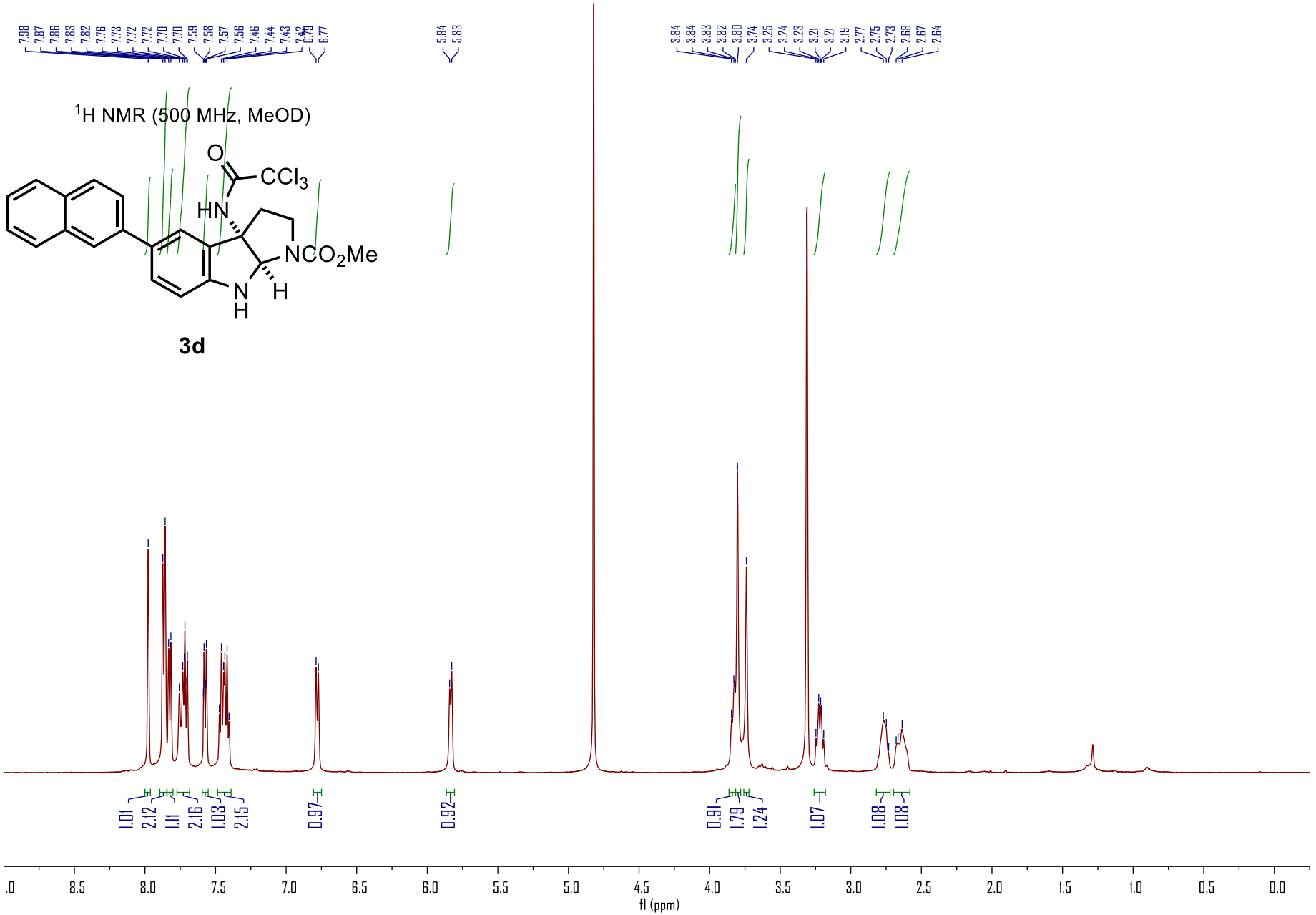


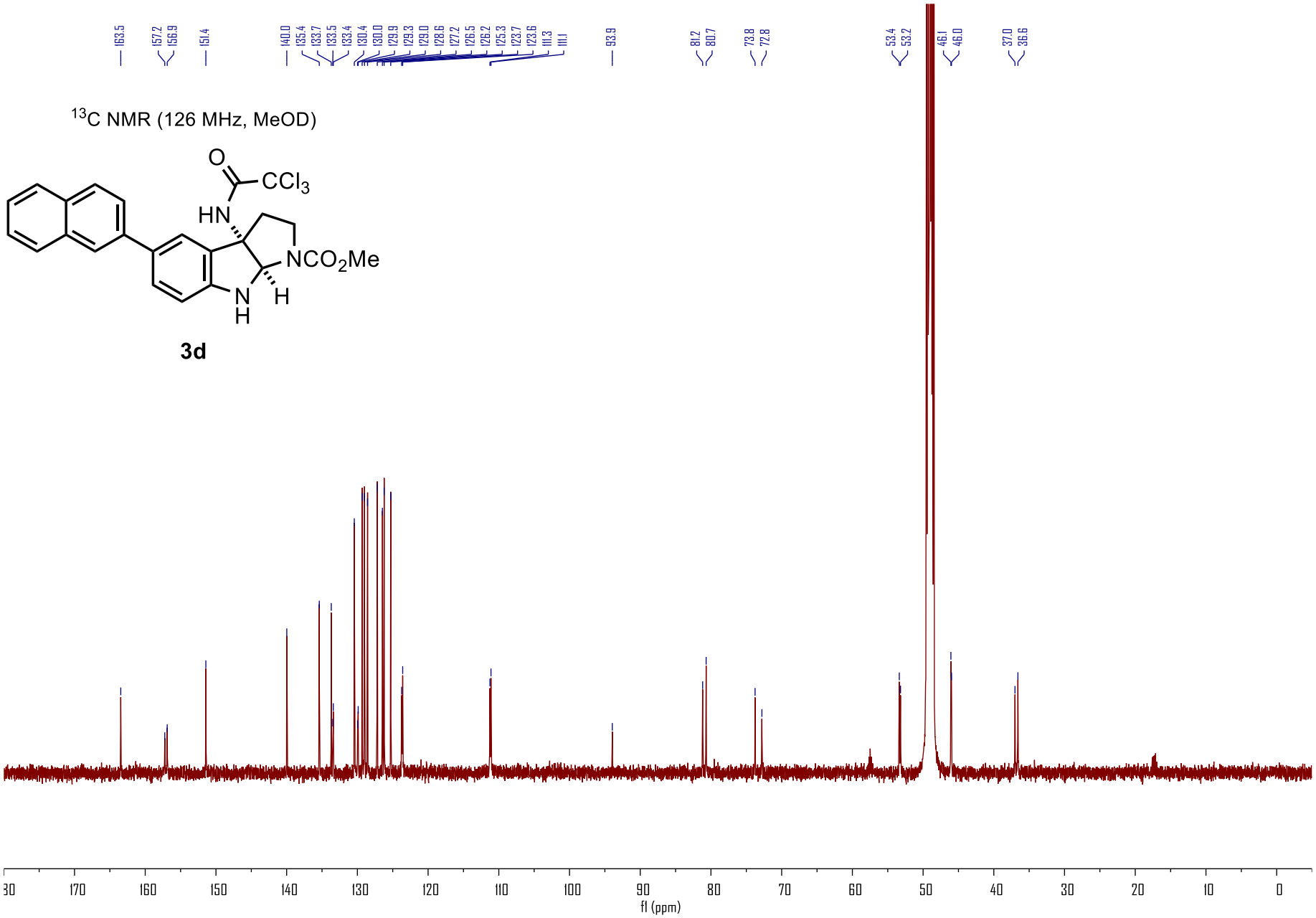

7.14
7.10
7.04
7.02
6.80
6.76
6.61
6.59
5.69
5.67
3.91
3.89
3.87
3.77
3.70
3.16
3.14
3.14
3.13
3.12
3.11
3.11
3.10
3.09
3.01
3.00
2.99
2.97
2.96
2.96
2.96
2.95
2.94
2.93
2.92
2.49
2.48
2.47
2.45
2.41
2.40
2.38
2.37
2.30
^{1}H NMR (500 MHz, $CDCl_3$)
O
CCl_3
HN
Me
NCO_2Me
N
H
H
3b
1.01
1.07
1.03
1.05
1.00
0.45
1.93
1.85
1.10
1.17
1.14
3.25
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

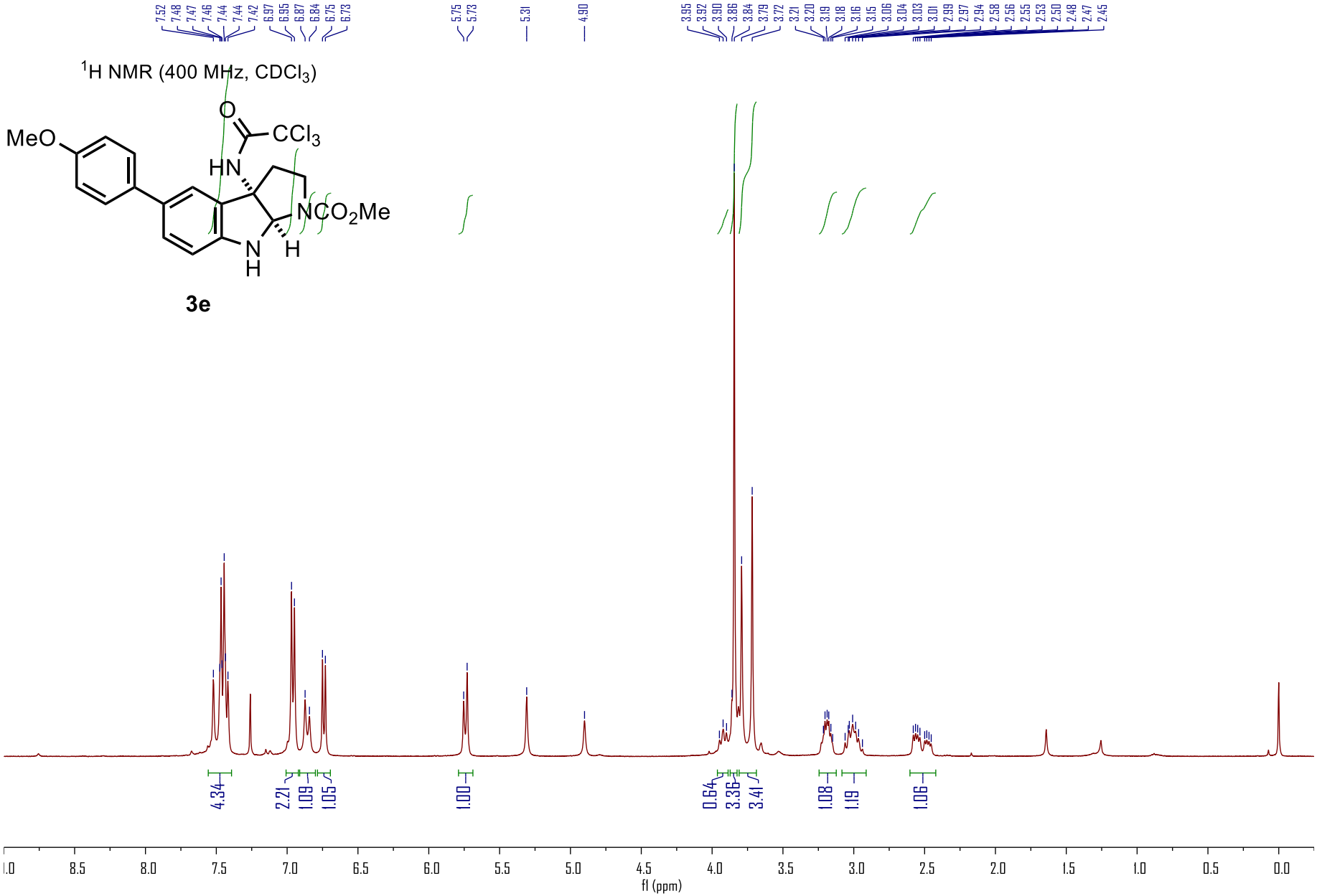

161.0
155.6
154.7
147.7
147.5
131.8
131.7
129.7
129.5
127.2
127.0
124.2
123.9
110.7
110.5
92.3
78.5
72.1
71.0
52.9
52.6
45.5
45.3
32.7
32.6
21.0
^{13}C NMR (101 MHz, CDCl$_3$)
O
CCl$_3$
HN
Me
NCO$_2$Me
N
H
H
3b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

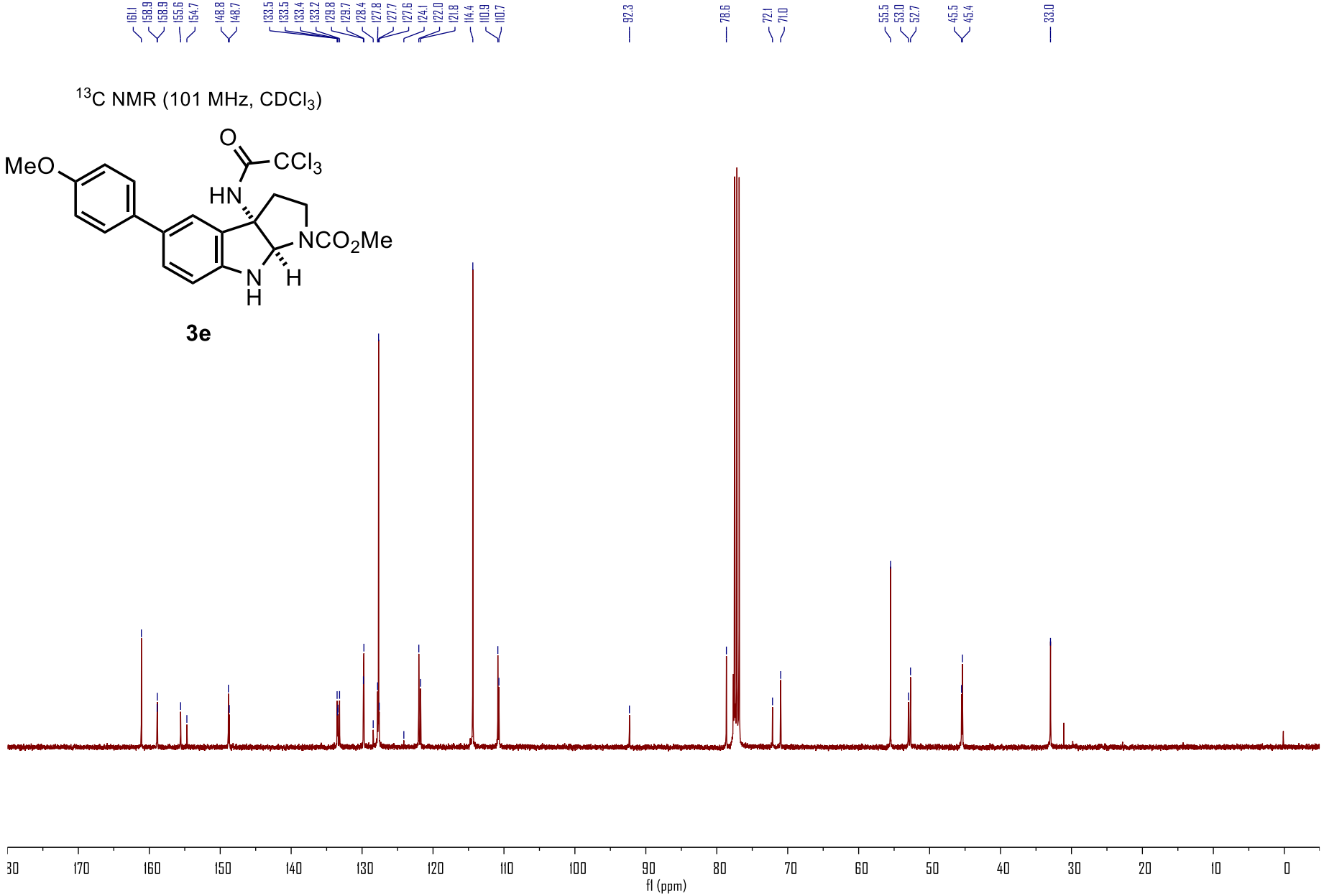

7.57
7.54
7.52
7.49
7.48
7.43
7.42
7.40
7.32
7.31
7.29
6.87
6.84
6.77
6.76
5.76
5.74
3.95
3.93
3.91
3.84
3.82
3.80
3.72
3.23
3.22
3.21
3.20
3.19
3.17
3.16
3.06
3.04
3.01
2.99
2.97
2.95
2.59
2.57
2.56
2.55
2.51
2.49
2.48
2.47
^{1}H NMR (500 MHz, $CDCl_3$)
O
CCl_3
HN
NCO_2Me
N
H
H
3c
3.20
1.24
2.21
1.16
0.85
1.03
1.00
0.42
1.90
1.83
1.15
1.21
1.21
f1 (ppm)


161.15
155.62
154.70
149.29
149.17
140.87
140.81
133.72
133.49
130.28
130.22
128.99
127.90
127.66
126.94
126.89
126.67
122.45
122.20
110.89
110.73
92.32
78.69
72.13
70.98
53.02
52.73
45.52
45.40
33.06
33.03
^{13}C NMR (126 MHz, CDCl$_3$)
O
CCl$_3$
HN
NCO$_2$Me
N
H
H
3c
f1 (ppm)

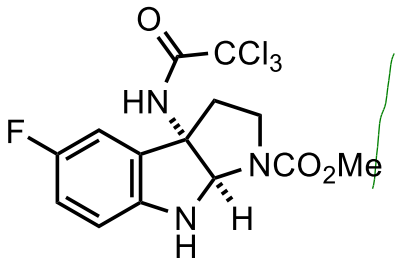

7.98
7.87
7.86
7.83
7.82
7.76
7.73
7.72
7.72
7.70
7.70
7.59
7.58
7.57
7.56
7.46
7.44
7.43
7.42
6.78
6.77
5.84
5.83
3.84
3.84
3.83
3.82
3.80
3.74
3.25
3.24
3.23
3.21
3.21
3.19
2.77
2.75
2.73
2.68
2.67
2.64
1H NMR (500 MHz, MeOD)
O
CCl3
HN
NCO2Me
N
H
H
3d
1.01
2.12
1.11
2.16
1.03
2.15
0.97
0.92
0.91
1.79
1.24
1.07
1.08
1.08
f1 (ppm)


163.5
157.2
156.9
151.4
140.0
135.4
133.7
133.5
133.4
130.4
130.0
129.9
129.3
129.0
128.6
127.2
126.5
126.2
125.3
123.7
123.6
111.3
111.1
93.9
81.2
80.7
73.8
72.8
53.4
53.2
46.1
46.0
37.0
36.6
^{13}C NMR (126 MHz, MeOD)
O
CCl$_3$
HN
NCO$_2$Me
N
H
H
3d
f1 (ppm)

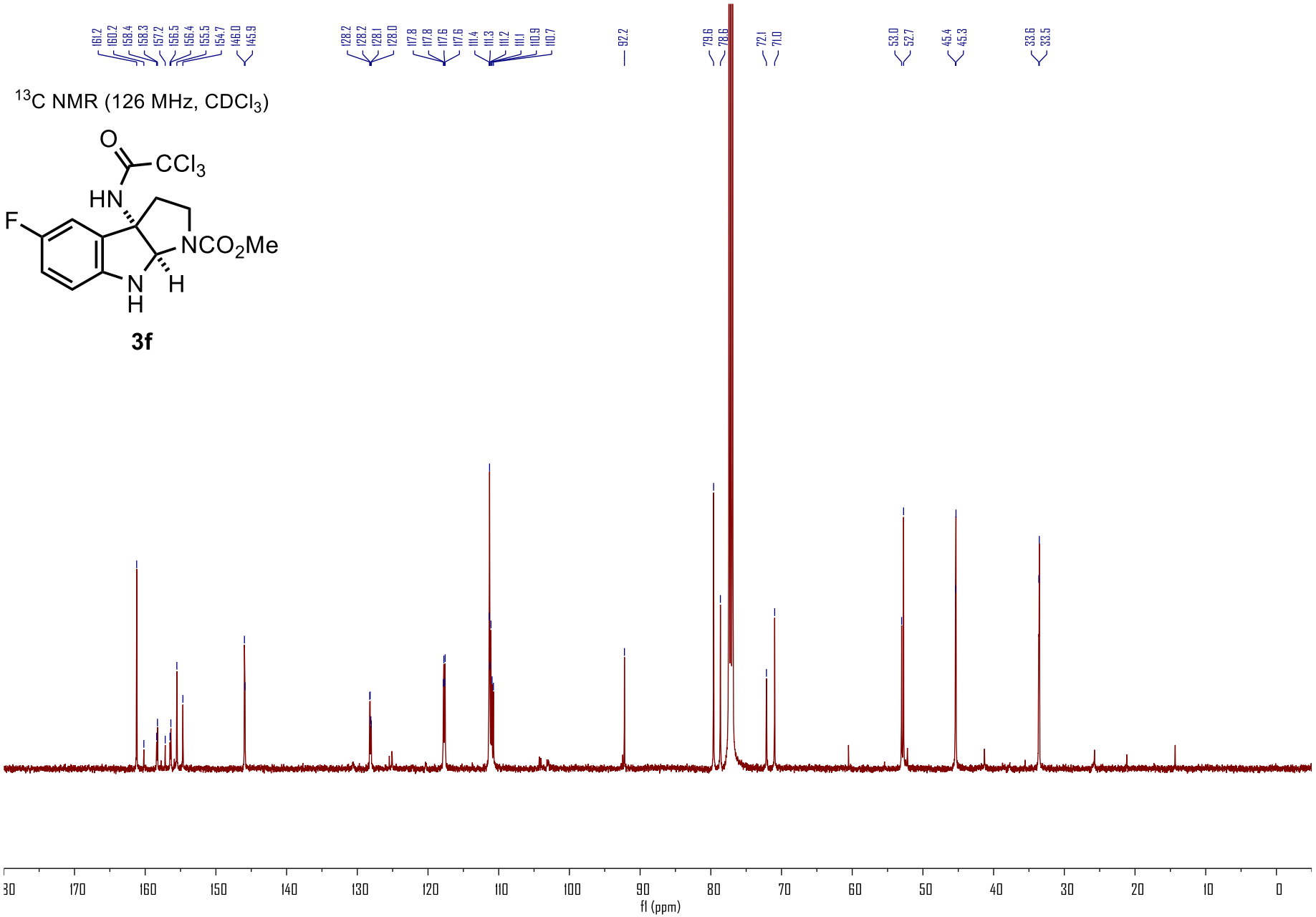

7.52
7.48
7.47
7.46
7.44
7.44
7.42
6.97
6.95
6.87
6.84
6.75
6.73
5.75
5.73
5.31
4.90
3.95
3.92
3.90
3.86
3.84
3.79
3.72
3.21
3.20
3.19
3.18
3.16
3.15
3.06
3.04
3.03
3.01
2.99
2.97
2.94
2.58
2.56
2.55
2.53
2.50
2.48
2.47
2.45
1H NMR (400 MHz, CDCl3)
MeO
O
CCl3
HN
NCO2Me
N
H
H
3e
4.34
2.21
1.09
1.05
1.00
0.64
3.36
3.41
1.08
1.19
1.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.1
158.9
158.9
155.6
154.7
148.8
148.7
133.5
133.5
133.4
133.2
129.8
129.7
128.4
127.8
127.7
127.6
124.1
122.0
121.8
114.4
110.9
110.7
92.3
78.6
72.1
71.0
55.5
53.0
52.7
45.5
45.4
33.0
^{13}C NMR (101 MHz, $CDCl_3$)
MeO
O
CCl_3
HN
NCO_2Me
N
H
H
3e
f1 (ppm)

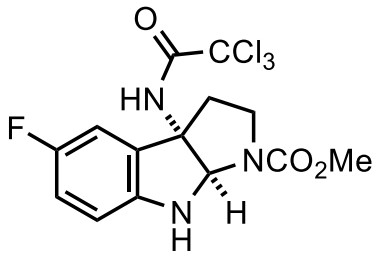
^{1}H NMR (500 MHz, $CDCl_3$)



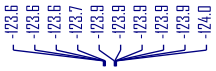
3f

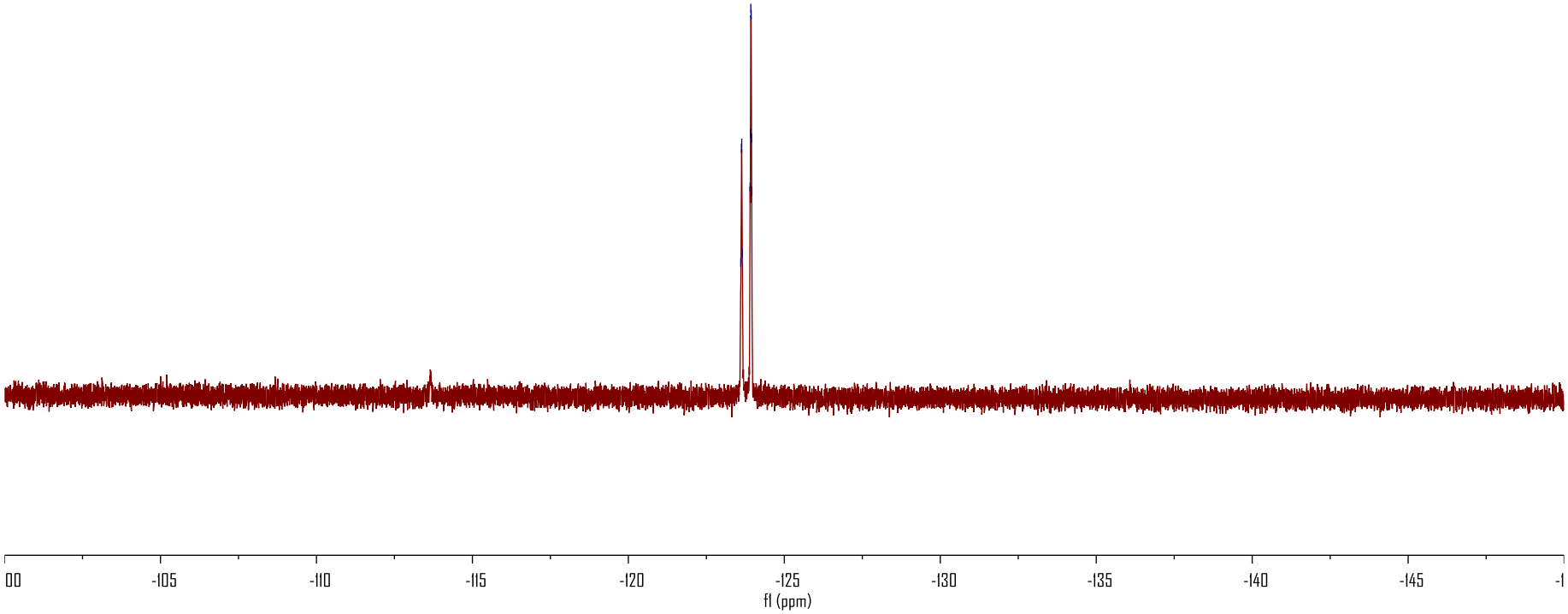

161.2
160.2
158.4
158.3
157.2
156.5
156.4
155.5
154.7
146.0
145.9
128.2
128.2
128.1
128.0
117.8
117.8
117.6
117.6
111.4
111.3
111.2
111.1
110.9
110.7
92.2
79.6
78.6
72.1
71.0
53.0
52.7
45.4
45.3
33.6
33.5
^{13}C NMR (126 MHz, $CDCl_3$)
O
CCl_3
HN
F
NCO_2Me
N
H
H
3f
f1 (ppm)

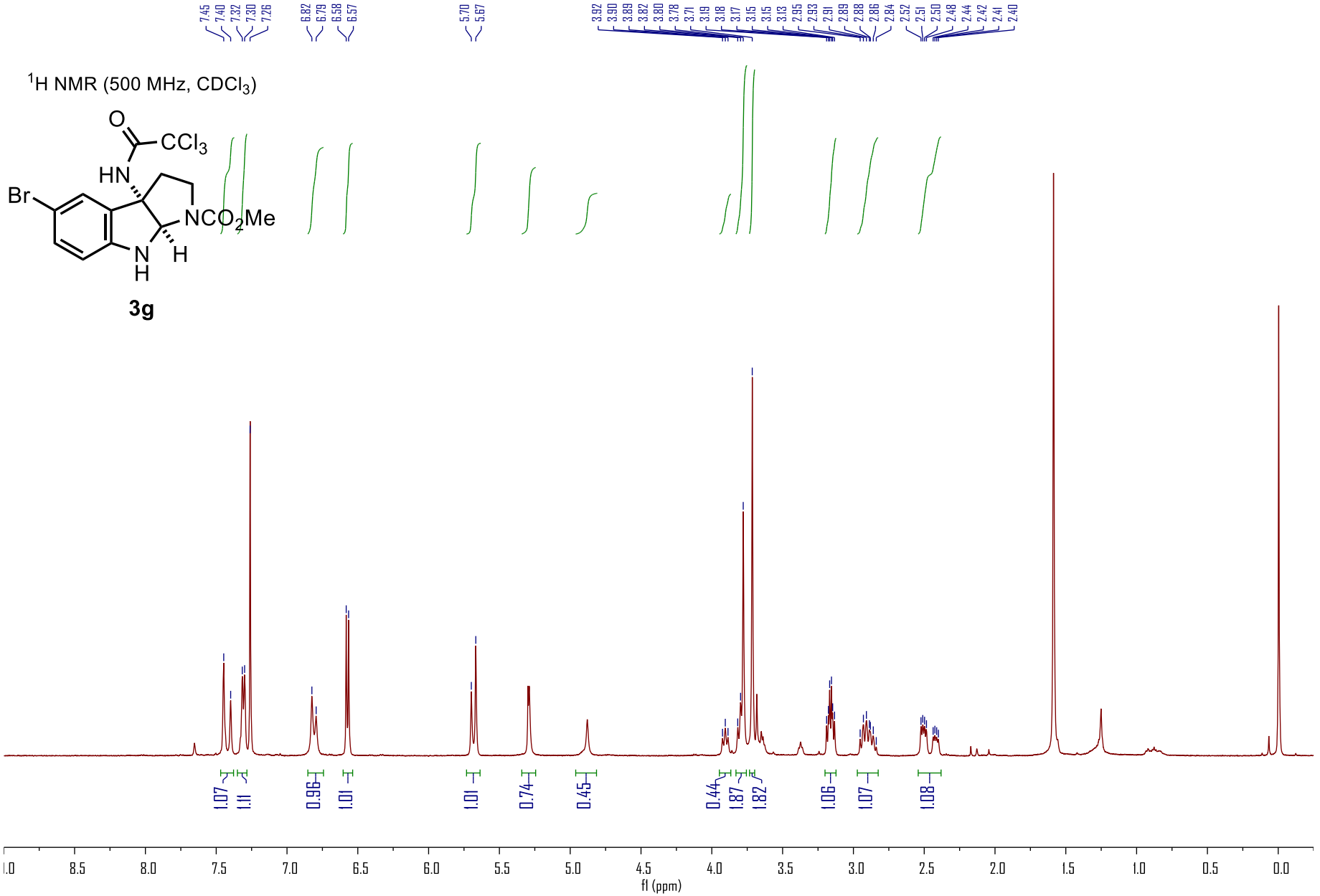
^{19}F NMR (376 MHz, $CDCl_3$)

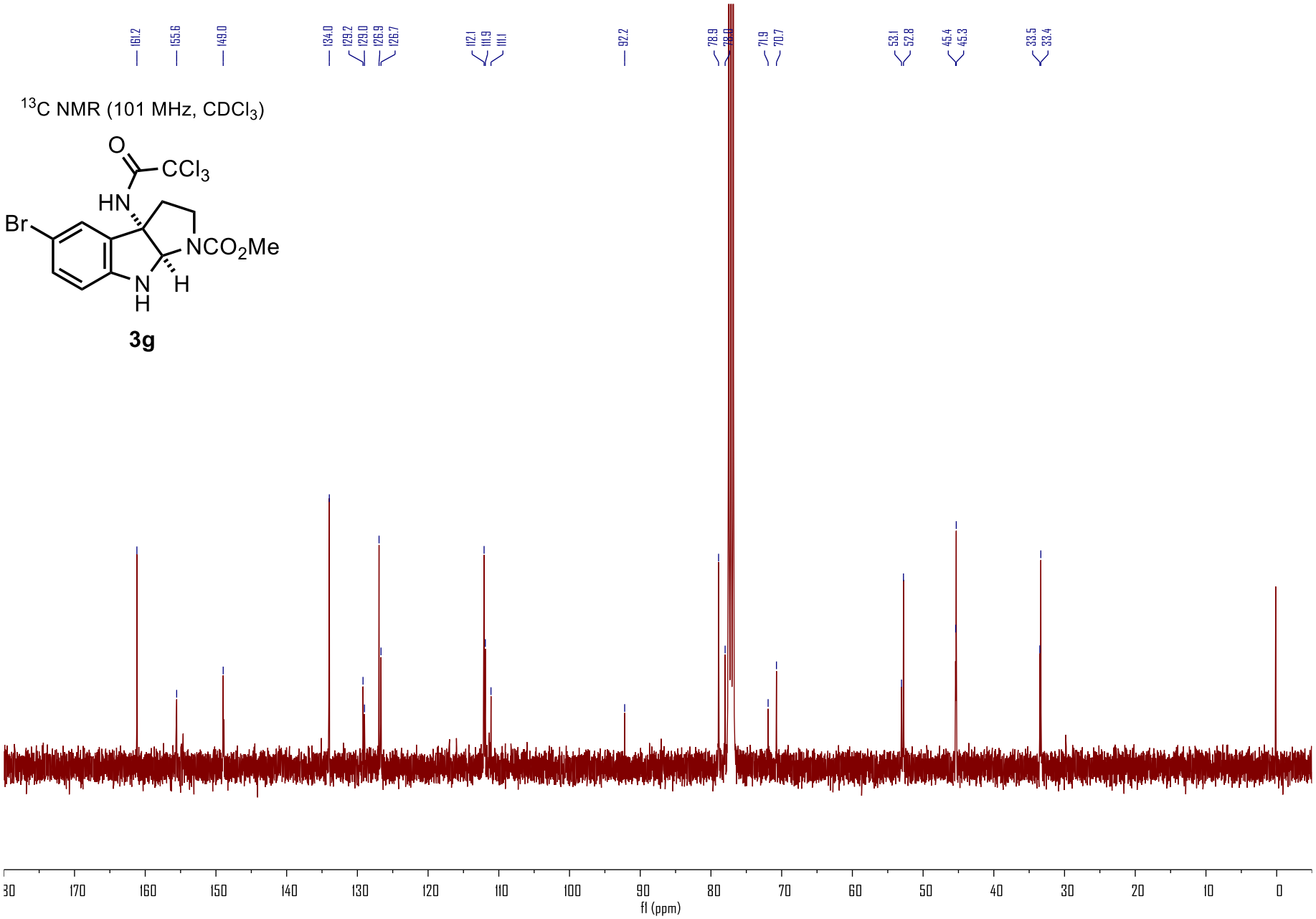


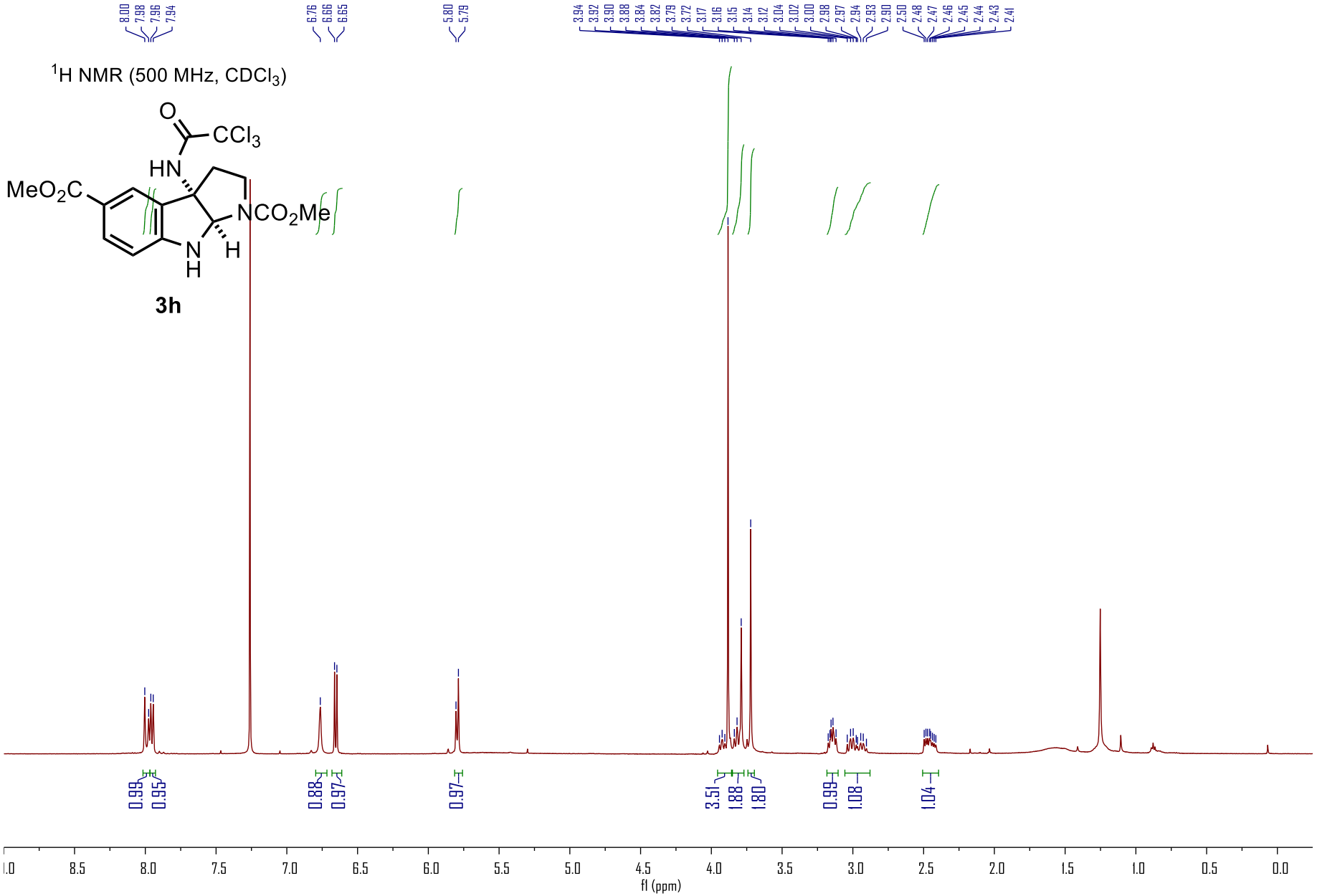
3f

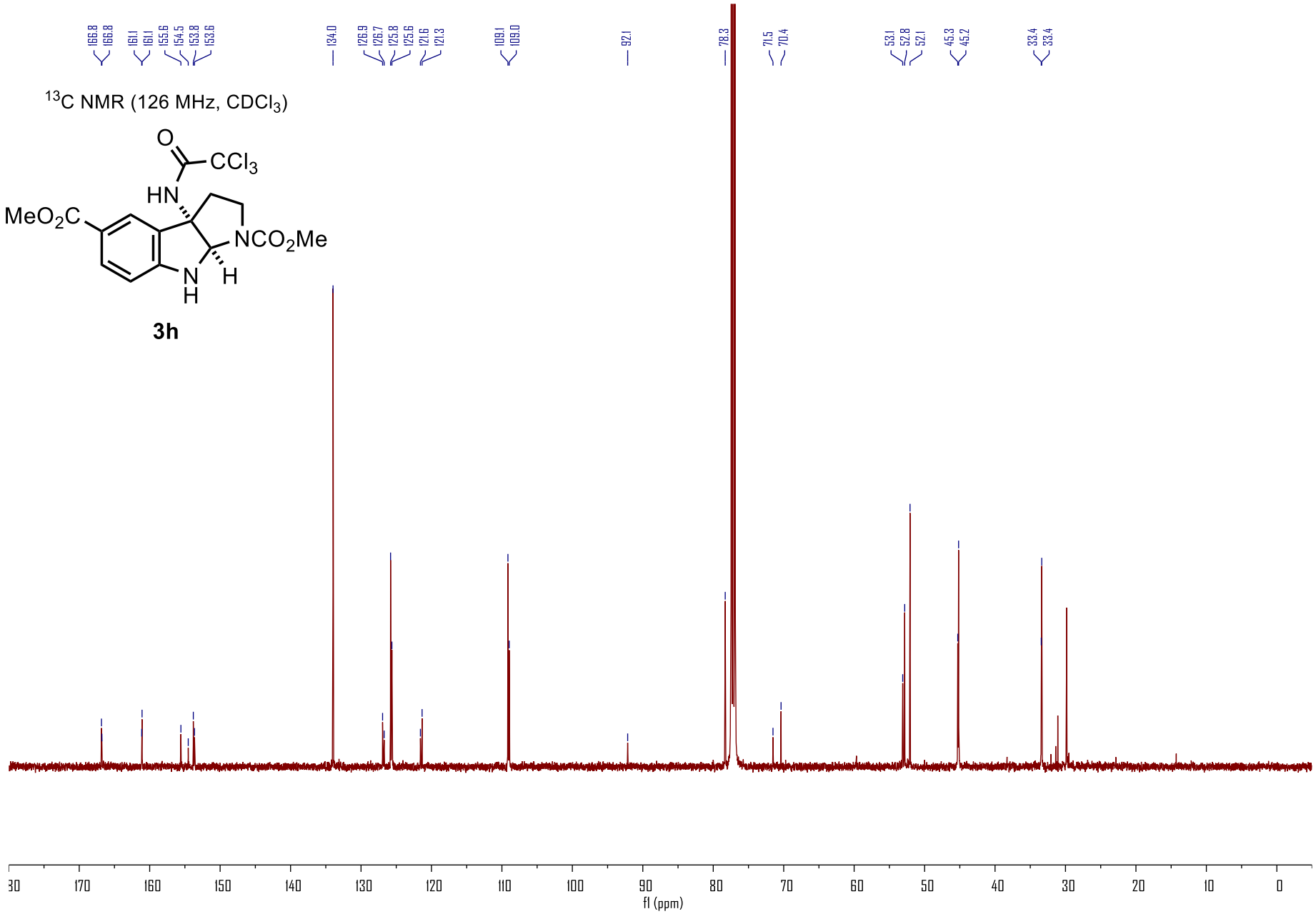




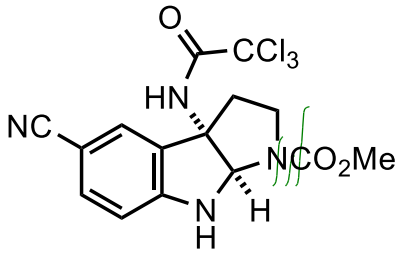

^{1}H NMR (500 MHz, $CDCl_3$)
O
CCl_3
HN
Br
NCO_2Me
N
H
H
3g
7.45
7.40
7.32
7.30
7.26
6.82
6.79
6.58
6.57
5.70
5.67
3.92
3.90
3.89
3.82
3.80
3.78
3.71
3.19
3.18
3.17
3.15
3.15
3.13
2.95
2.93
2.91
2.89
2.88
2.86
2.84
2.52
2.51
2.50
2.48
2.44
2.42
2.41
2.40
1.07
1.11
0.96
1.01
1.01
0.74
0.45
0.44
1.87
1.82
1.06
1.07
1.08
f1 (ppm)


161.2
155.6
149.0
134.0
129.2
129.0
126.9
126.7
112.1
111.9
111.1
92.2
78.9
78.6
71.9
70.7
53.1
52.8
45.4
45.3
33.5
33.4
^{13}C NMR (101 MHz, CDCl$_3$)
O
CCl$_3$
HN
Br
NCO$_2$Me
N
H
H
3g
f1 (ppm)

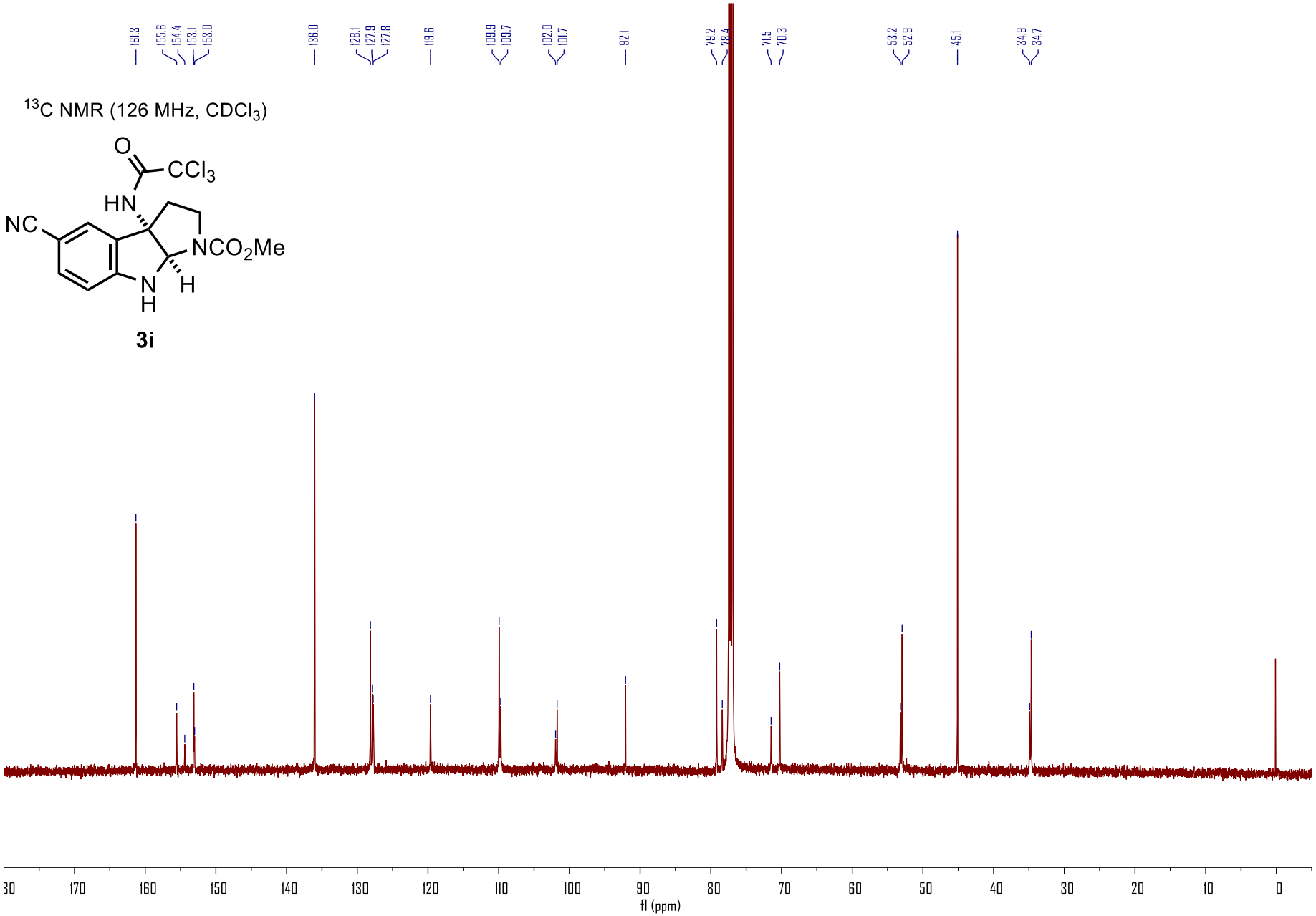

8.00
7.98
7.96
7.94
6.76
6.66
6.65
5.80
5.79
3.94
3.92
3.90
3.88
3.84
3.82
3.79
3.72
3.17
3.16
3.15
3.14
3.12
3.04
3.02
3.00
2.98
2.97
2.94
2.93
2.90
2.50
2.48
2.47
2.46
2.45
2.44
2.43
2.41
^{1}H NMR (500 MHz, $CDCl_3$)
O
CCl_3
HN
MeO_2C
NCO_2Me
N
H
H
3h
0.99
0.95
0.88
0.97
0.97
3.51
1.88
1.80
0.99
1.08
1.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

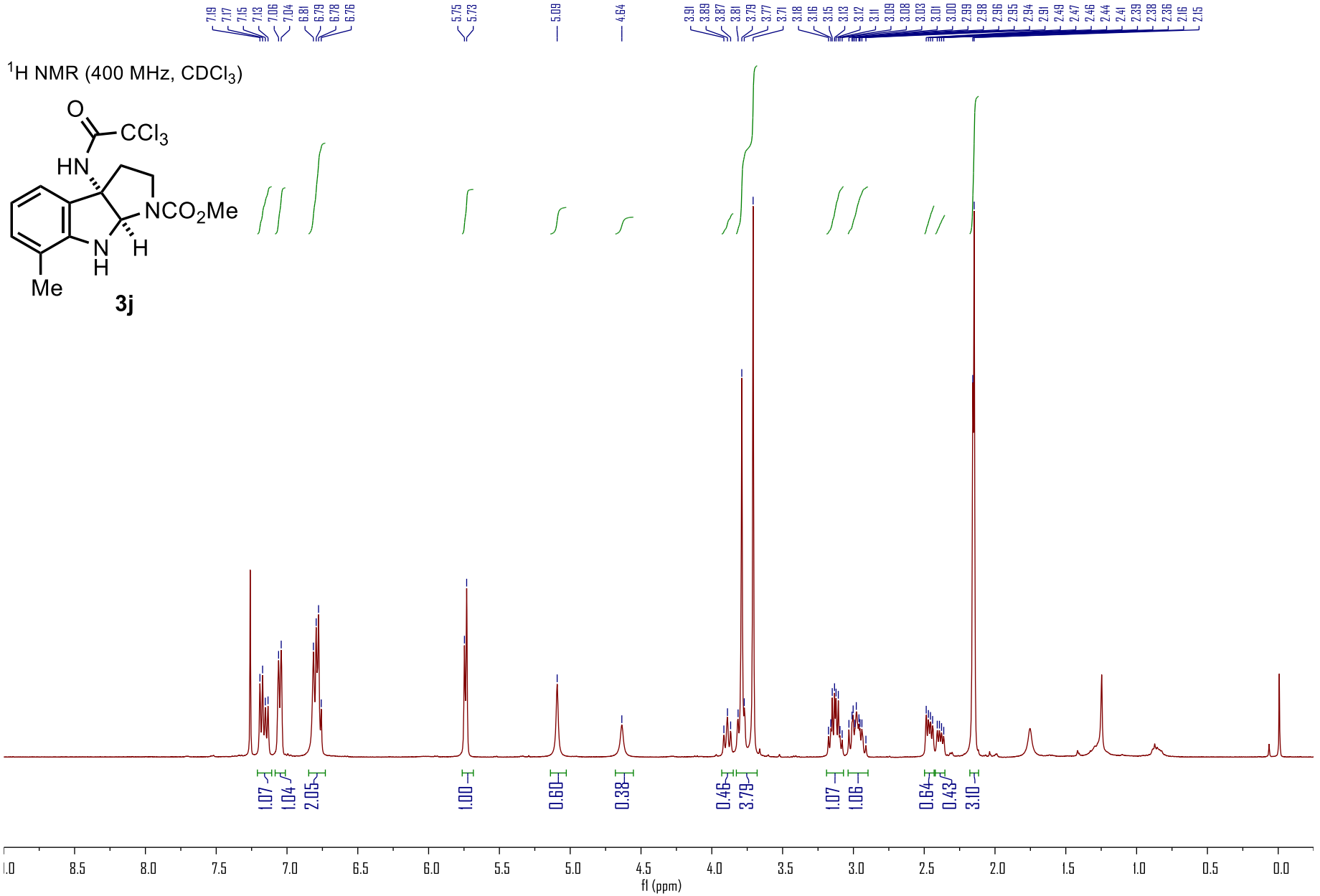

166.8
166.8
161.1
161.1
155.6
154.5
153.8
153.6
134.0
126.9
126.7
125.8
125.6
121.6
121.3
109.1
109.0
92.1
78.3
71.5
70.4
53.1
52.8
52.1
45.3
45.2
33.4
33.4
^{13}C NMR (126 MHz, $CDCl_3$)
O
CCl_3
HN
MeO_2C
NCO_2Me
N
H
H
3h
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

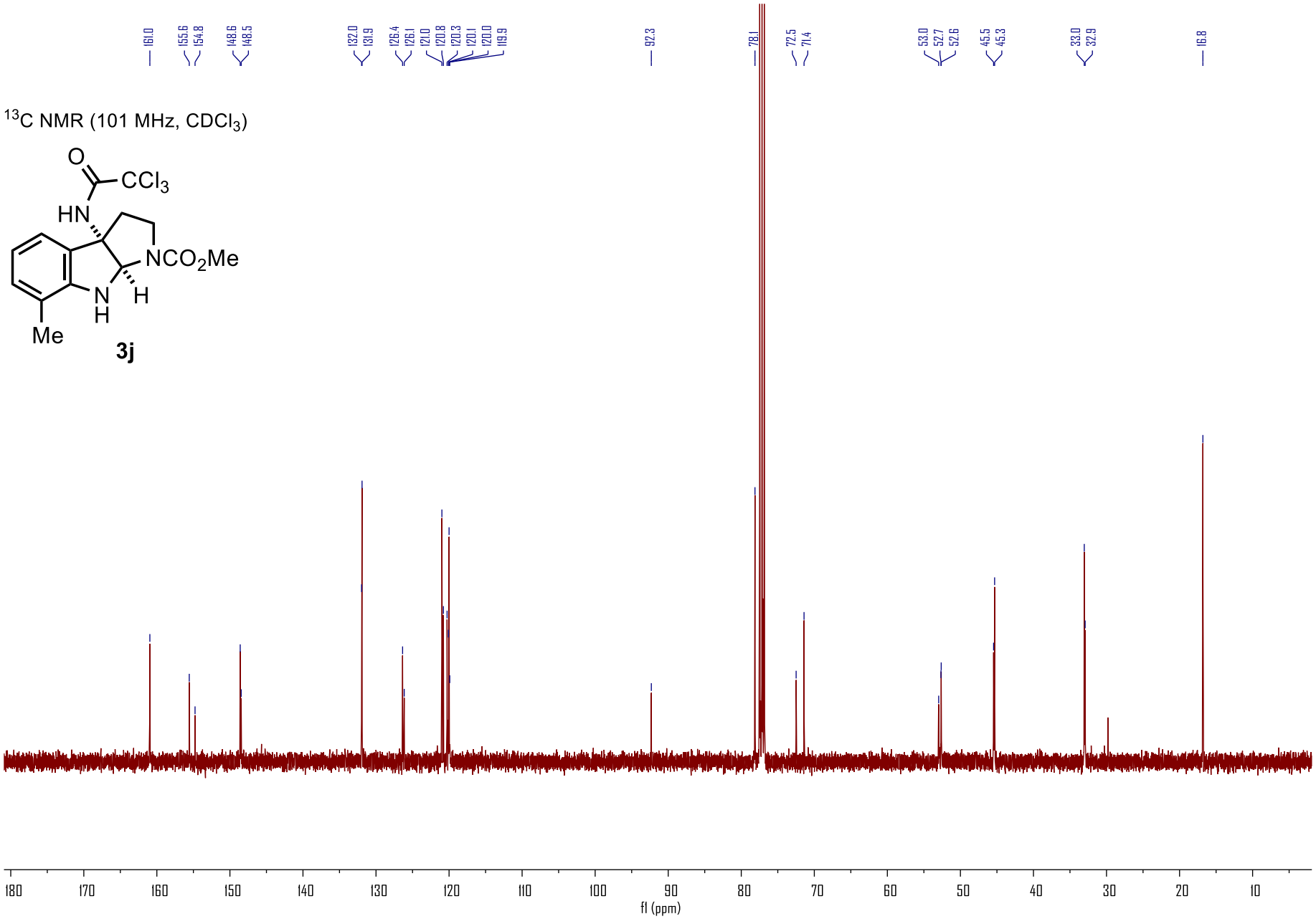
^{1}H NMR (500 MHz, $CDCl_3$)

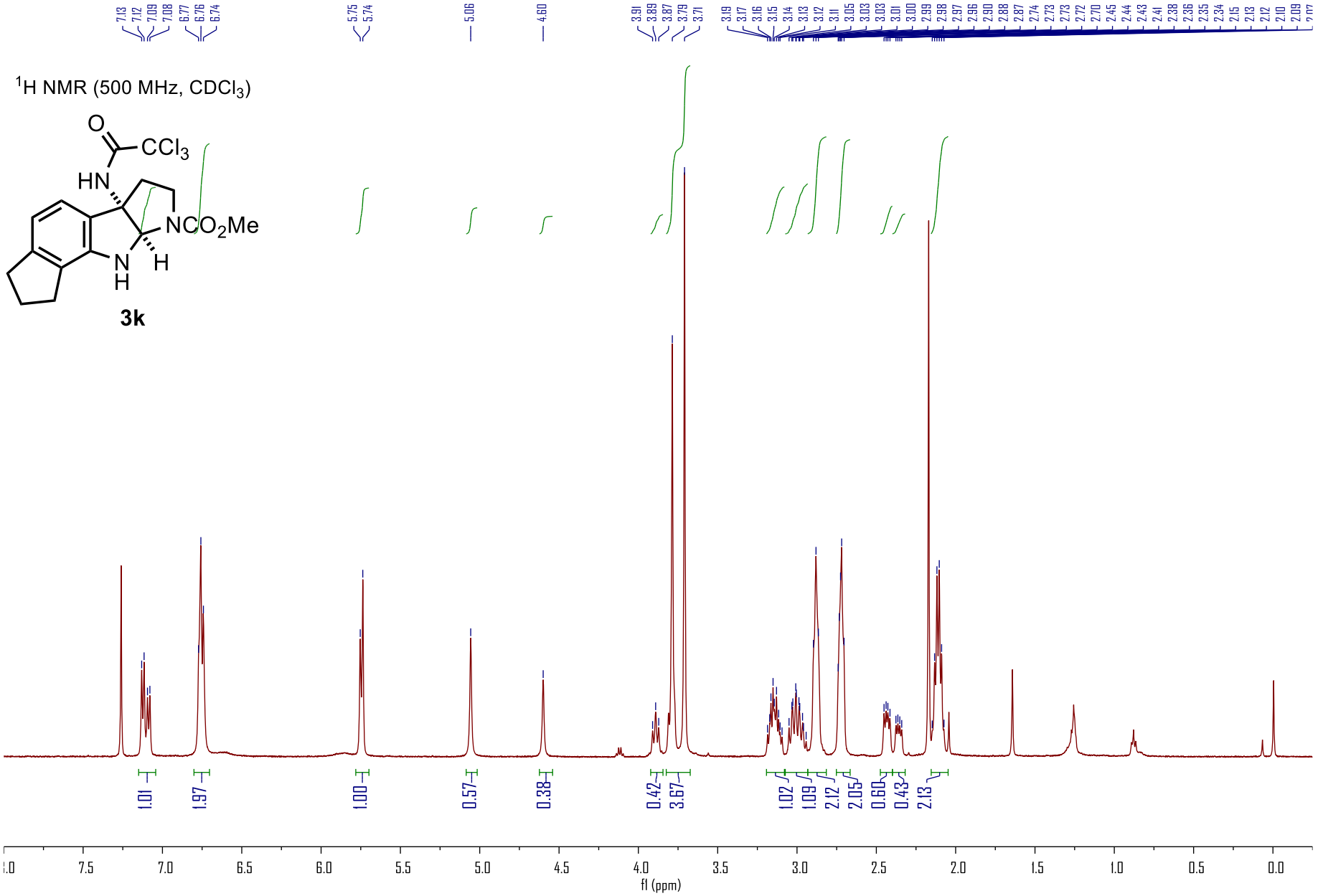


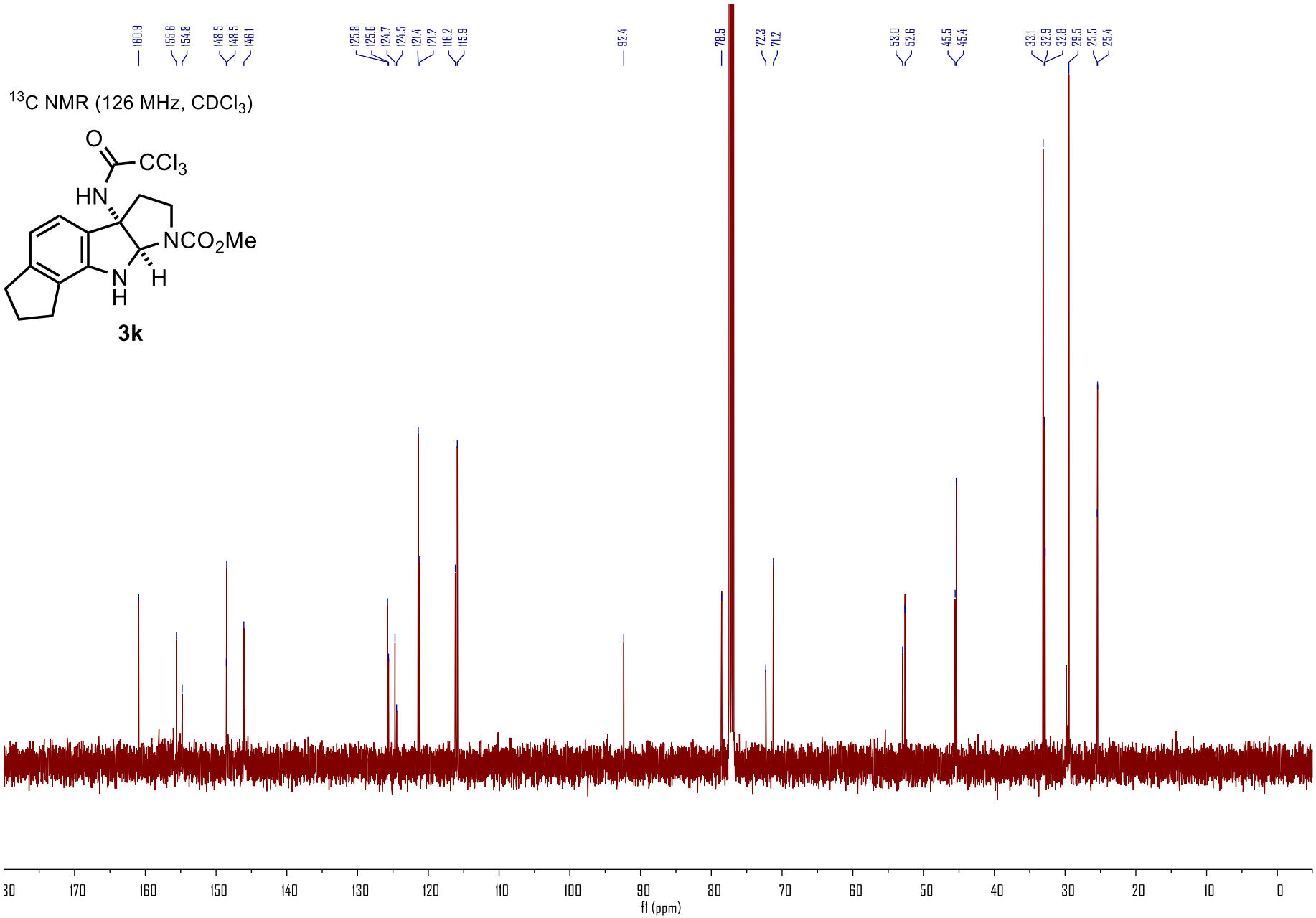
3i


161.3
155.6
154.4
153.1
153.0
136.0
128.1
127.9
127.8
119.6
109.9
109.7
102.0
101.7
92.1
79.2
78.4
71.5
70.3
53.2
52.9
45.1
34.9
34.7
^{13}C NMR (126 MHz, CDCl$_3$)
O
CCl$_3$
HN
NC
NCO$_2$Me
N
H
H
3i
f1 (ppm)

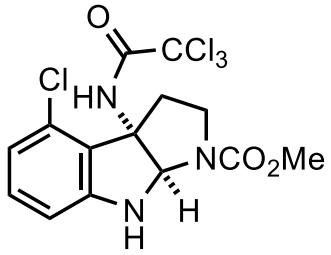

7.19
7.17
7.15
7.13
7.06
7.04
6.81
6.79
6.78
6.76
5.75
5.73
5.09
4.64
3.91
3.89
3.87
3.81
3.79
3.77
3.71
3.18
3.16
3.15
3.13
3.12
3.11
3.09
3.08
3.03
3.01
3.00
2.99
2.98
2.96
2.95
2.94
2.91
2.49
2.47
2.46
2.44
2.41
2.39
2.38
2.36
2.16
2.15
1H NMR (400 MHz, CDCl3)
O
CCl3
HN
NCO2Me
N
H
H
Me
3j
1.07
1.04
2.05
1.00
0.60
0.38
0.46
3.79
1.07
1.06
0.64
0.43
3.10
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.0
155.6
154.8
148.6
148.5
132.0
131.9
126.4
126.1
121.0
120.8
120.3
120.1
120.0
119.9
92.3
78.1
72.5
71.4
53.0
52.7
52.6
45.5
45.3
33.0
32.9
16.8
13C NMR (101 MHz, CDCl3)
O
CCl3
HN
NCO2Me
N
H
H
Me
3j
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

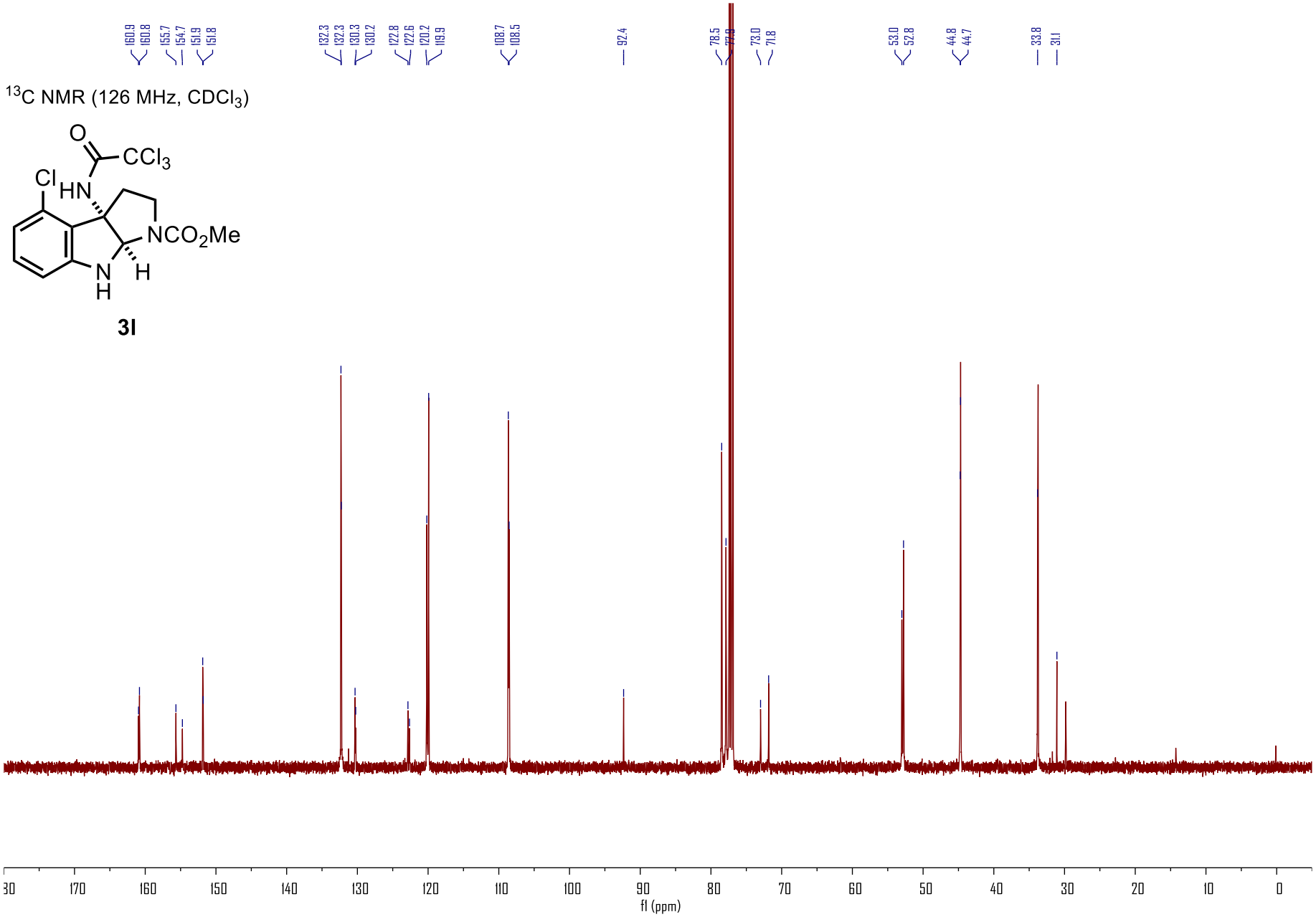

^{1}H NMR (500 MHz, $CDCl_3$)
O
CCl_3
HN
NCO_2Me
N
H
H
3k
7.13
7.12
7.09
7.08
6.77
6.76
6.74
5.75
5.74
5.06
4.60
3.91
3.89
3.87
3.79
3.71
3.19
3.17
3.16
3.15
3.14
3.13
3.12
3.11
3.05
3.03
3.03
3.01
3.00
2.99
2.98
2.97
2.96
2.90
2.88
2.87
2.74
2.73
2.73
2.72
2.70
2.45
2.44
2.43
2.41
2.38
2.36
2.35
2.34
2.15
2.13
2.12
2.10
2.09
1.01
1.97
1.00
0.57
0.38
0.42
3.67
1.02
1.09
2.12
2.05
0.60
0.43
2.13
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

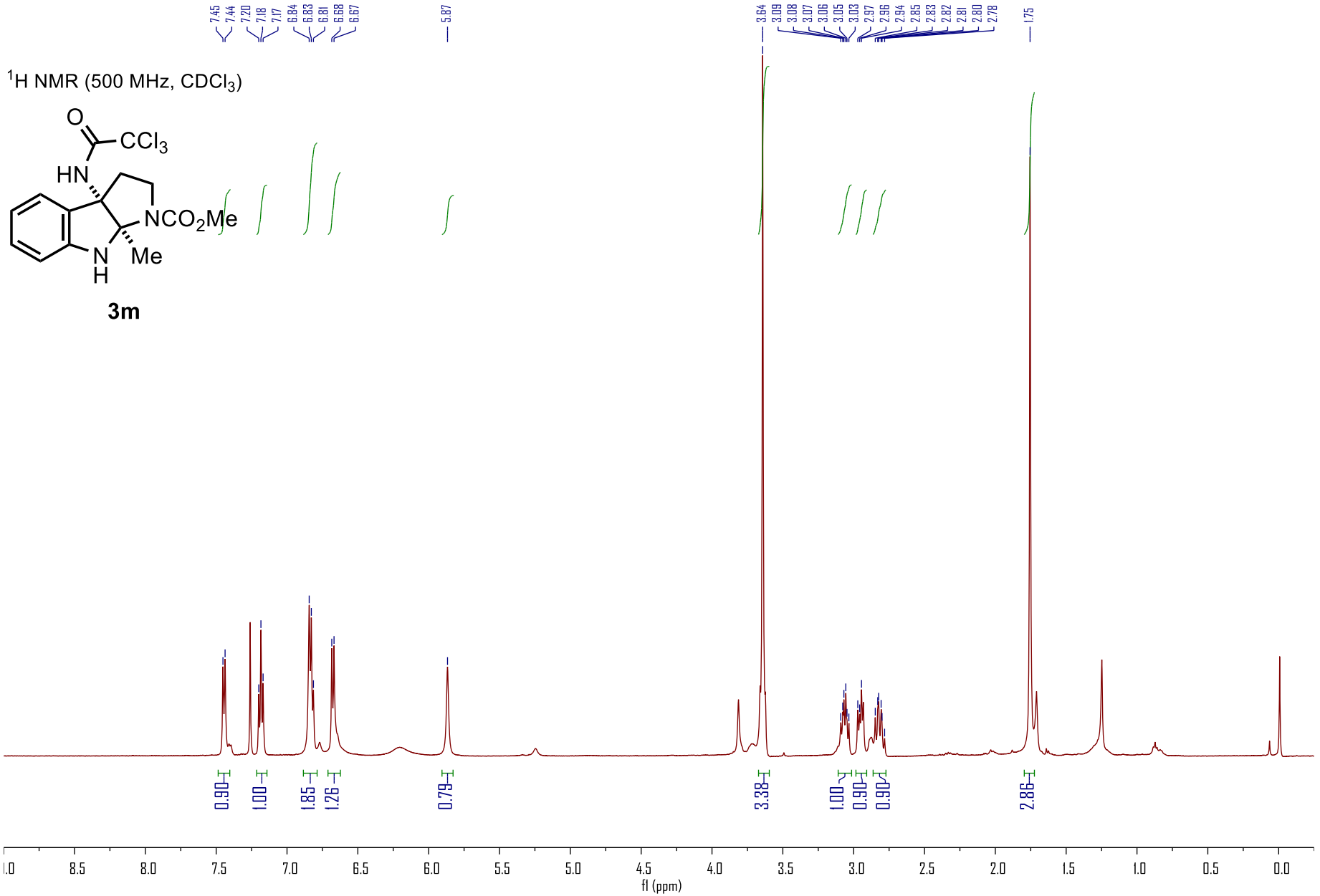

160.9
155.6
154.8
148.5
148.5
146.1
125.8
125.6
124.7
124.5
121.4
121.2
116.2
115.9
92.4
78.5
72.3
71.2
53.0
52.6
45.5
45.4
33.1
32.9
32.8
29.5
25.5
25.4
13C NMR (126 MHz, CDCl3)
O
CCl3
HN
NCO2Me
N
H
H
3k
f1 (ppm)

^{1}H NMR (500 MHz, $CDCl_3$)

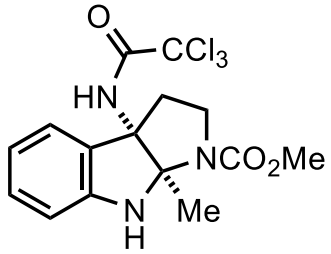


3l

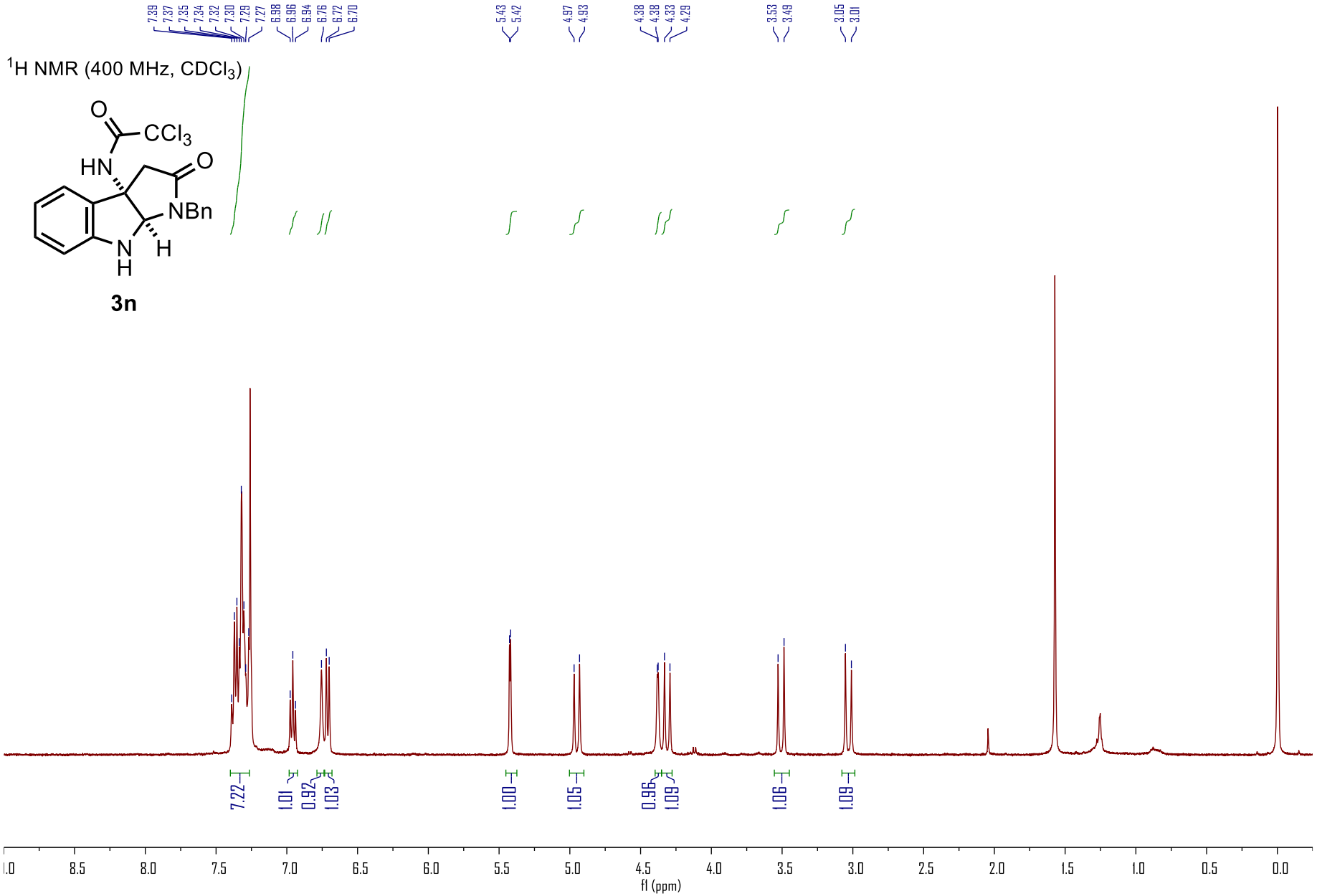

160.9
160.8
155.7
154.7
151.9
151.8
132.3
132.3
130.3
130.2
122.8
122.6
120.2
119.9
108.7
108.5
92.4
78.5
77.9
73.0
71.8
53.0
52.8
44.8
44.7
33.8
31.1
13C NMR (126 MHz, CDCl3)
O
CCl3
Cl
HN
NCO2Me
N
H
H
3l
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

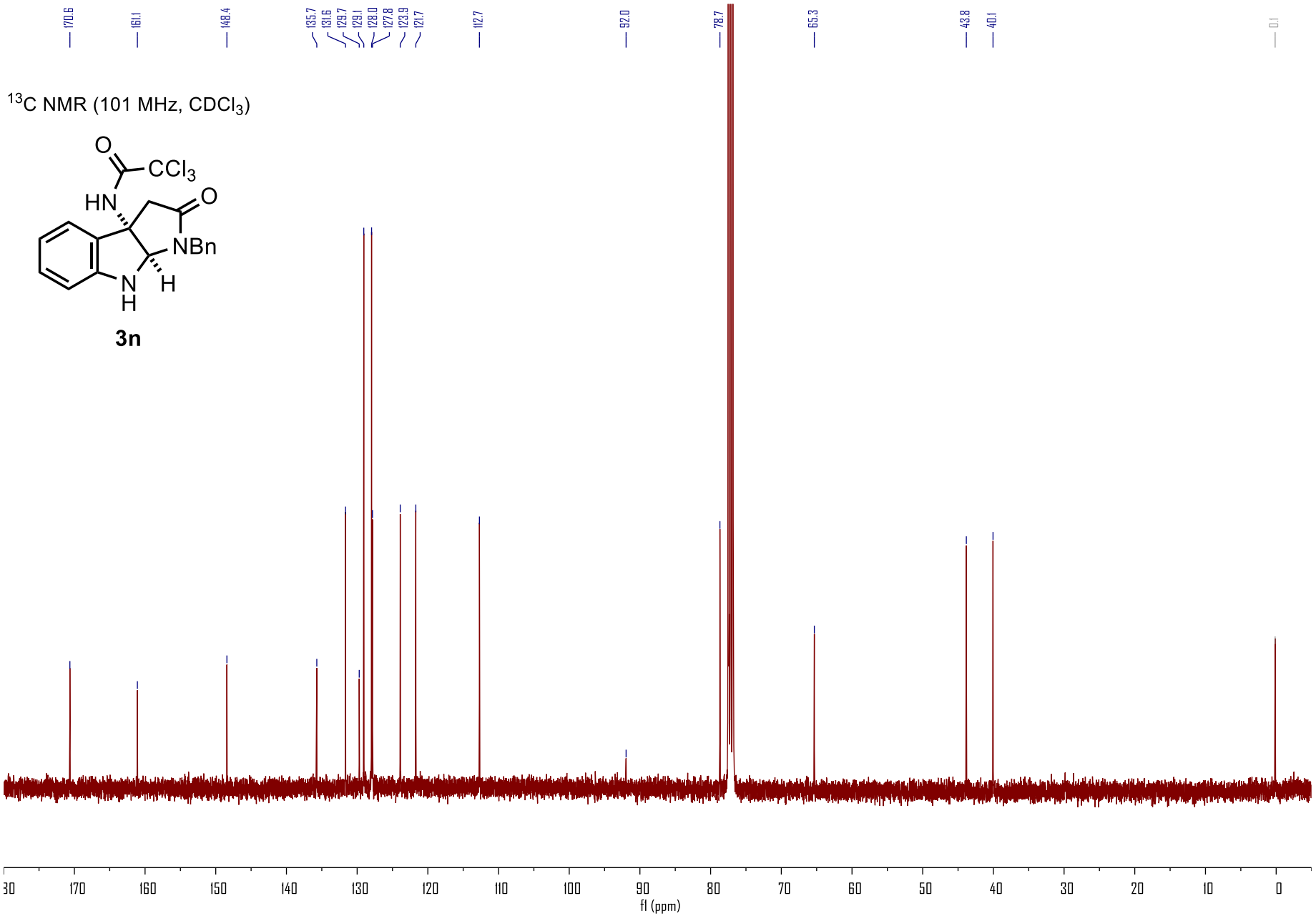

^{1}H NMR (500 MHz, $CDCl_3$)
O
CCl_3
HN
NCO_2Me
N
H
Me
3m
7.45
7.44
7.20
7.18
7.17
6.84
6.83
6.81
6.68
6.67
5.87
3.64
3.09
3.08
3.07
3.06
3.05
3.03
2.97
2.96
2.94
2.85
2.83
2.82
2.81
2.80
2.78
1.75
0.90
1.00
1.85
1.26
0.79
3.38
1.00
0.90
0.90
2.86
f1 (ppm)

^{13}C NMR (126 MHz, $CDCl_3$)

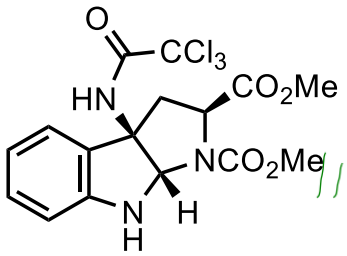


3m

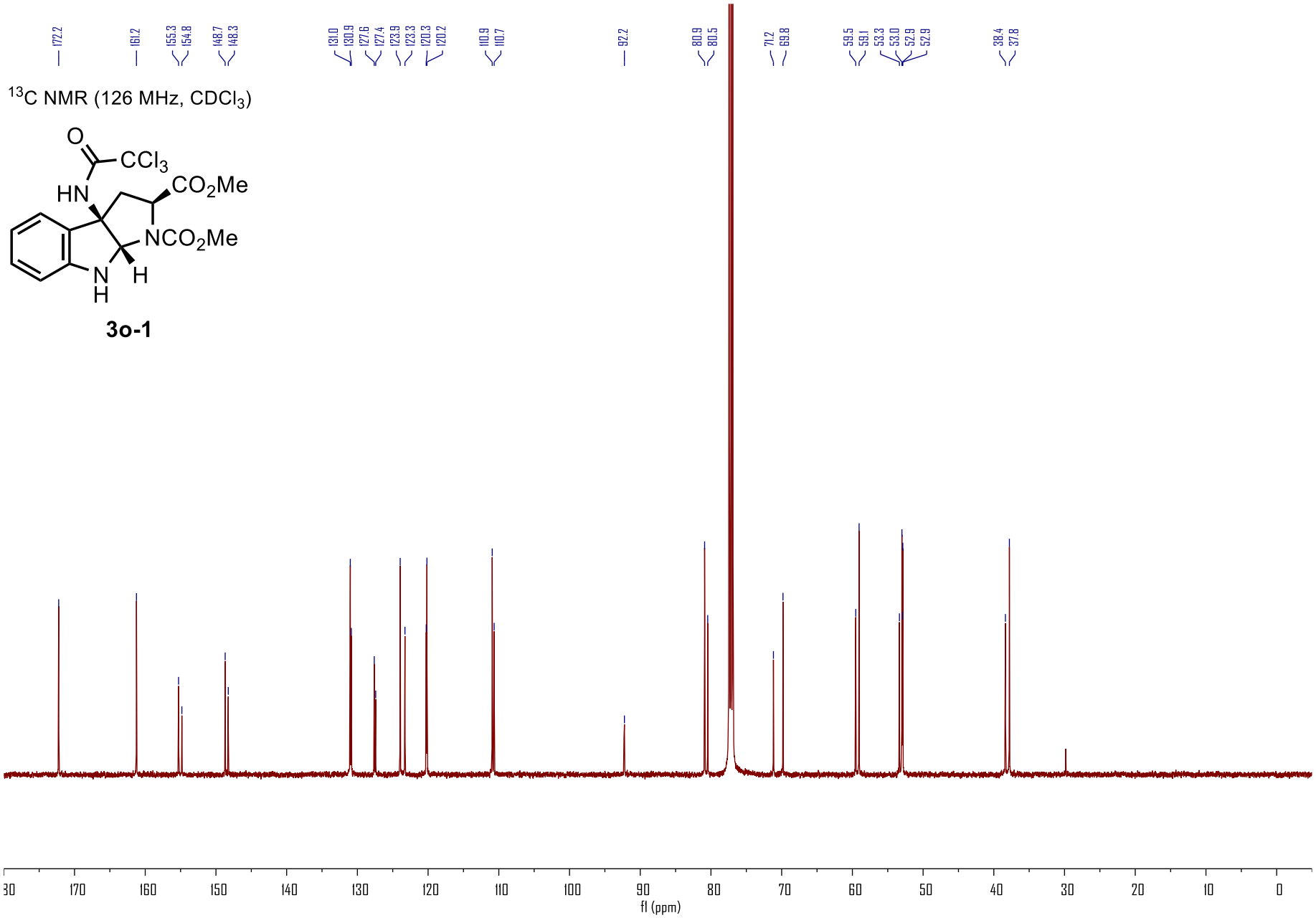

7.39
7.37
7.35
7.34
7.32
7.30
7.29
7.27
6.98
6.96
6.94
6.76
6.72
6.70
5.43
5.42
4.97
4.93
4.38
4.38
4.33
4.29
3.53
3.49
3.05
3.01
^{1}H NMR (400 MHz, $CDCl_3$)
O
CCl_3
HN
O
NBn
N
H
H
3n
7.22
1.01
0.92
1.03
1.00
1.05
0.96
1.09
1.06
1.09
f1 (ppm)

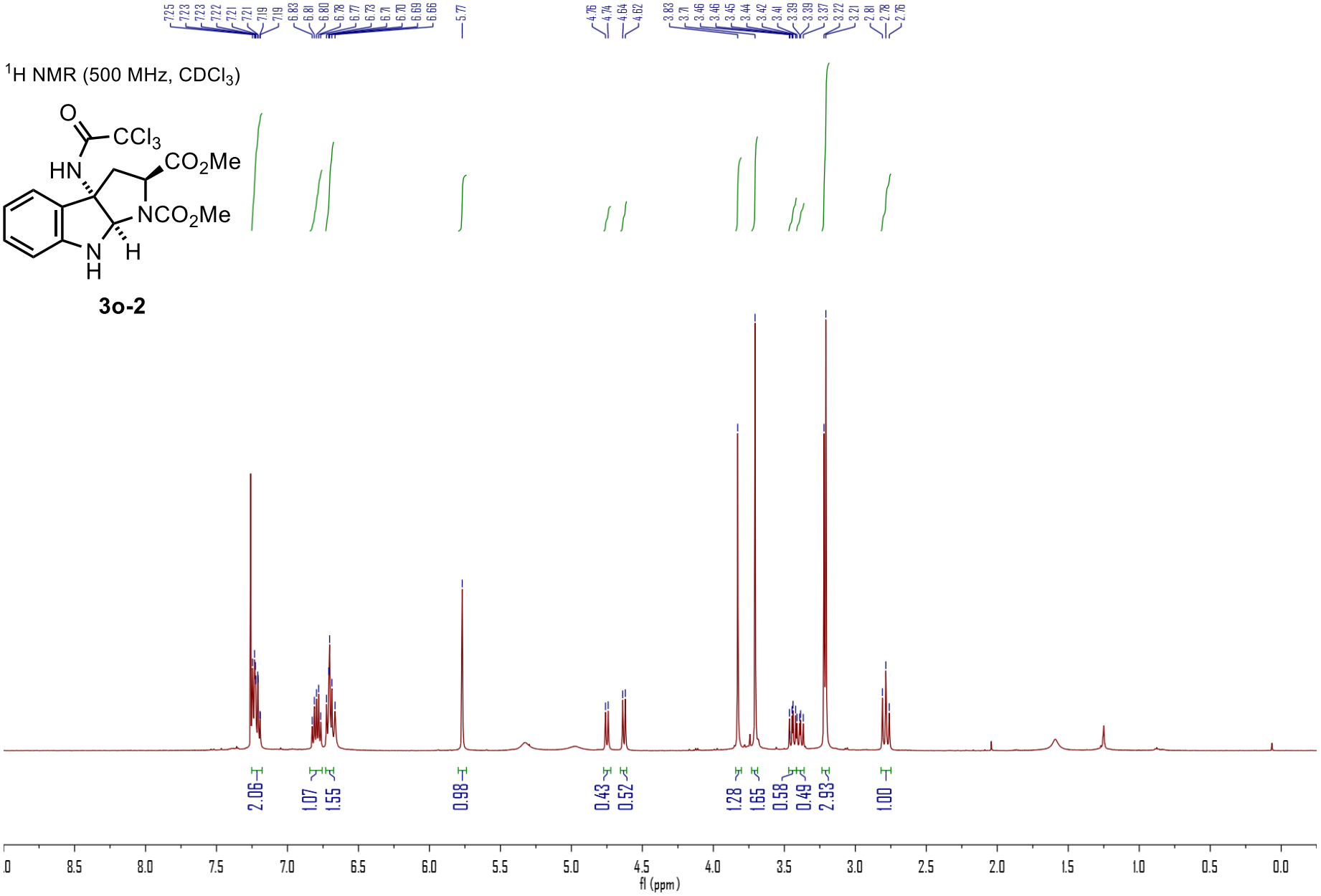

170.6
161.1
148.4
135.7
131.6
129.7
129.1
128.0
127.8
123.9
121.7
112.7
92.0
78.7
65.3
43.8
40.1
0.1
^{13}C NMR (101 MHz, $CDCl_3$)
O
CCl_3
HN
O
NBn
N
H
H
3n
f1 (ppm)

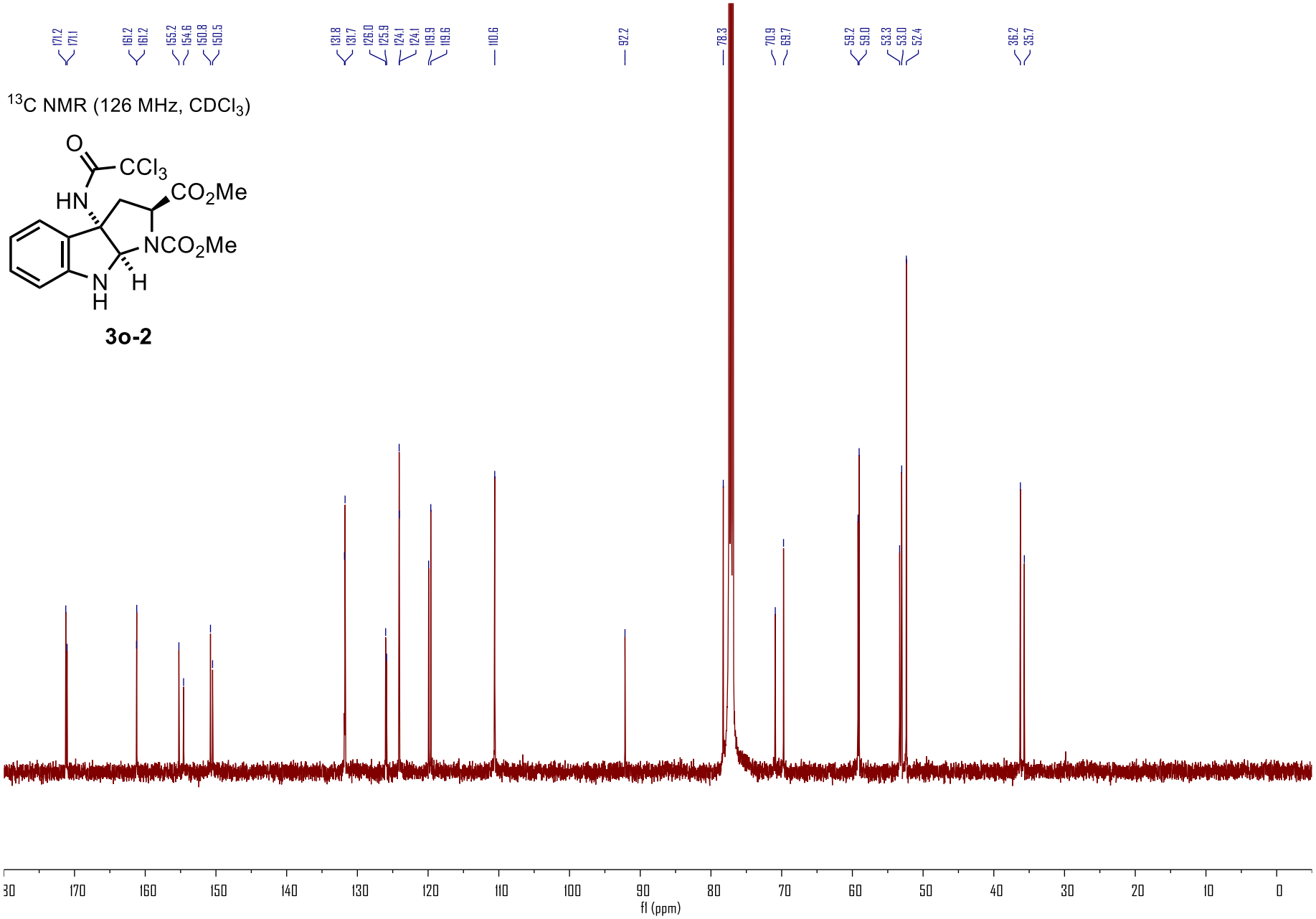
^{1}H NMR (500 MHz, $CDCl_3$)

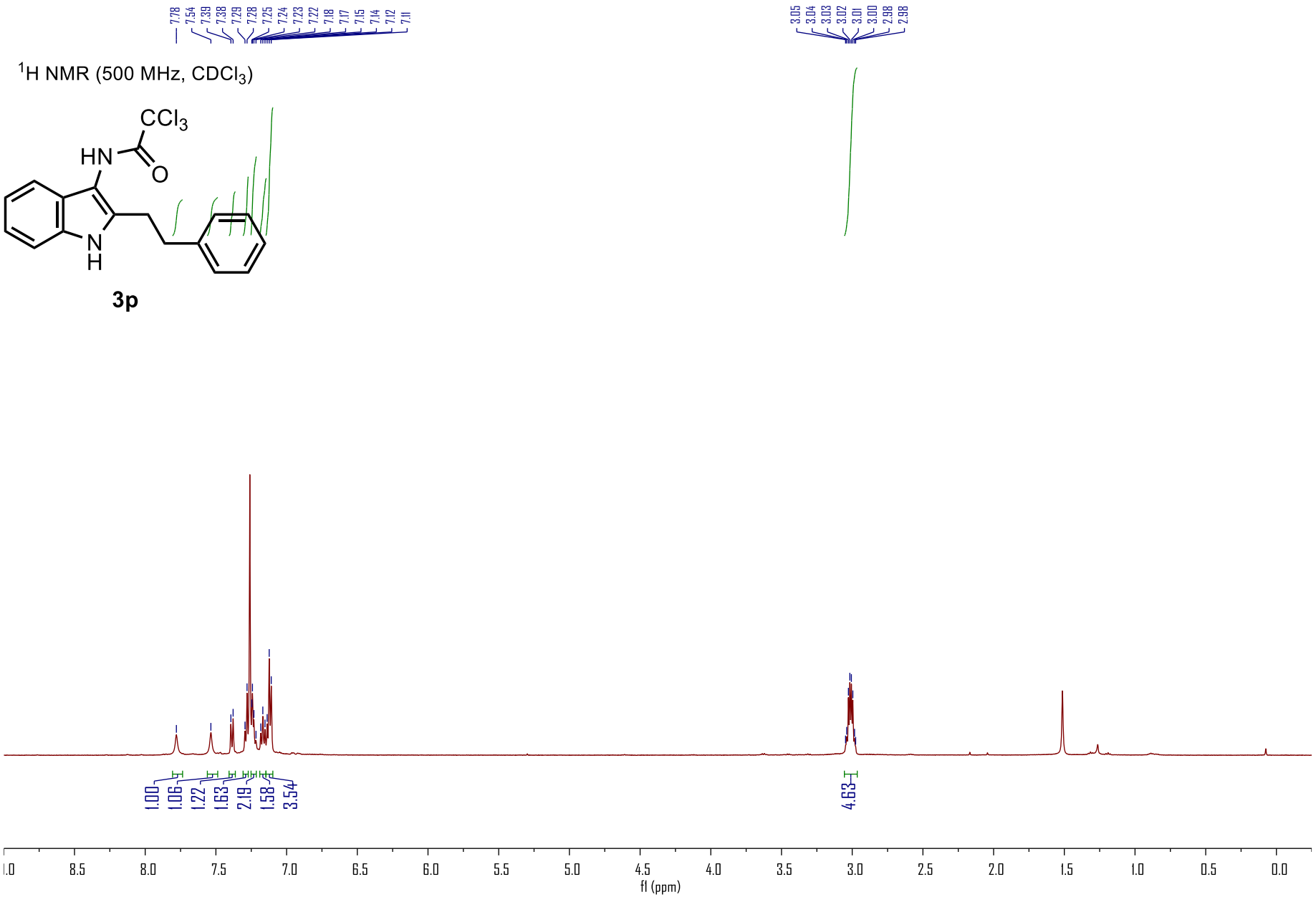


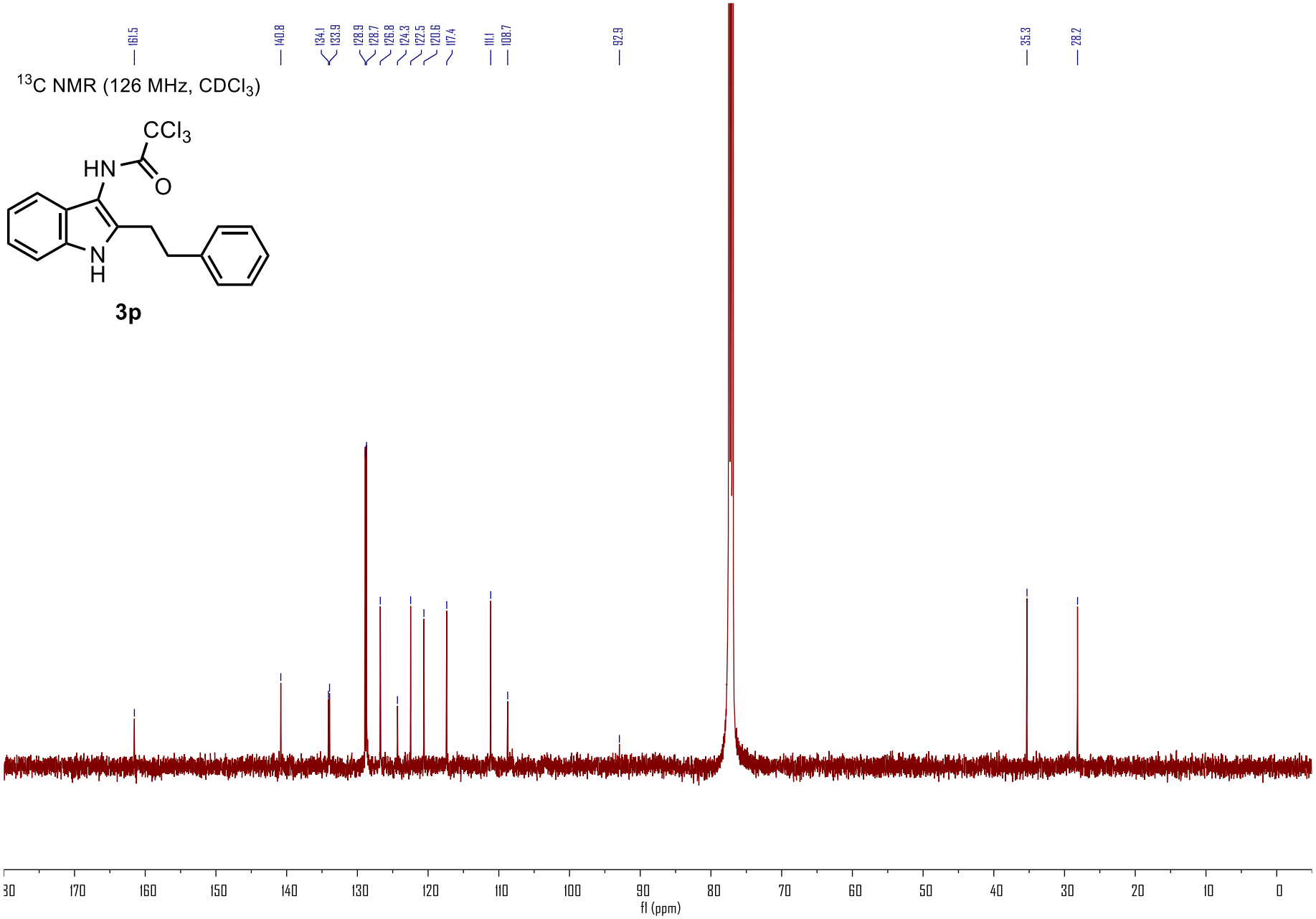
3o-1


172.2
161.2
155.3
154.8
148.7
148.3
131.0
130.9
127.6
127.4
123.9
123.3
120.3
120.2
110.9
110.7
92.2
80.9
80.5
71.2
69.8
59.5
59.1
53.3
53.0
52.9
52.9
38.4
37.8
13C NMR (126 MHz, CDCl3)
O
CCl3
HN
CO2Me
NCO2Me
N
H
H
3o-1
f1 (ppm)

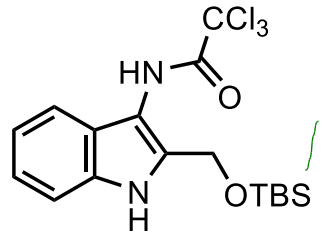

7.25
7.23
7.23
7.22
7.21
7.21
7.19
7.19
6.83
6.81
6.80
6.78
6.77
6.73
6.71
6.70
6.69
6.66
5.77
4.75
4.74
4.64
4.62
3.83
3.71
3.46
3.46
3.45
3.44
3.42
3.41
3.39
3.39
3.37
3.22
3.21
2.81
2.78
2.76
1H NMR (500 MHz, CDCl3)
O
CCl3
HN
CO2Me
NCO2Me
N
H
H
3o-2
2.06
1.07
1.55
0.98
0.43
0.52
1.28
1.65
0.58
0.49
2.93
1.00
f1 (ppm)


171.2
171.1
161.2
161.2
155.2
154.6
150.8
150.5
131.8
131.7
126.0
125.9
124.1
124.1
119.9
119.6
110.6
92.2
78.3
70.9
69.7
59.2
59.0
53.3
53.0
52.4
36.2
35.7
^{13}C NMR (126 MHz, CDCl$_3$)
O
CCl$_3$
HN
CO$_2$Me
NCO$_2$Me
N
H
H
3o-2
f1 (ppm)

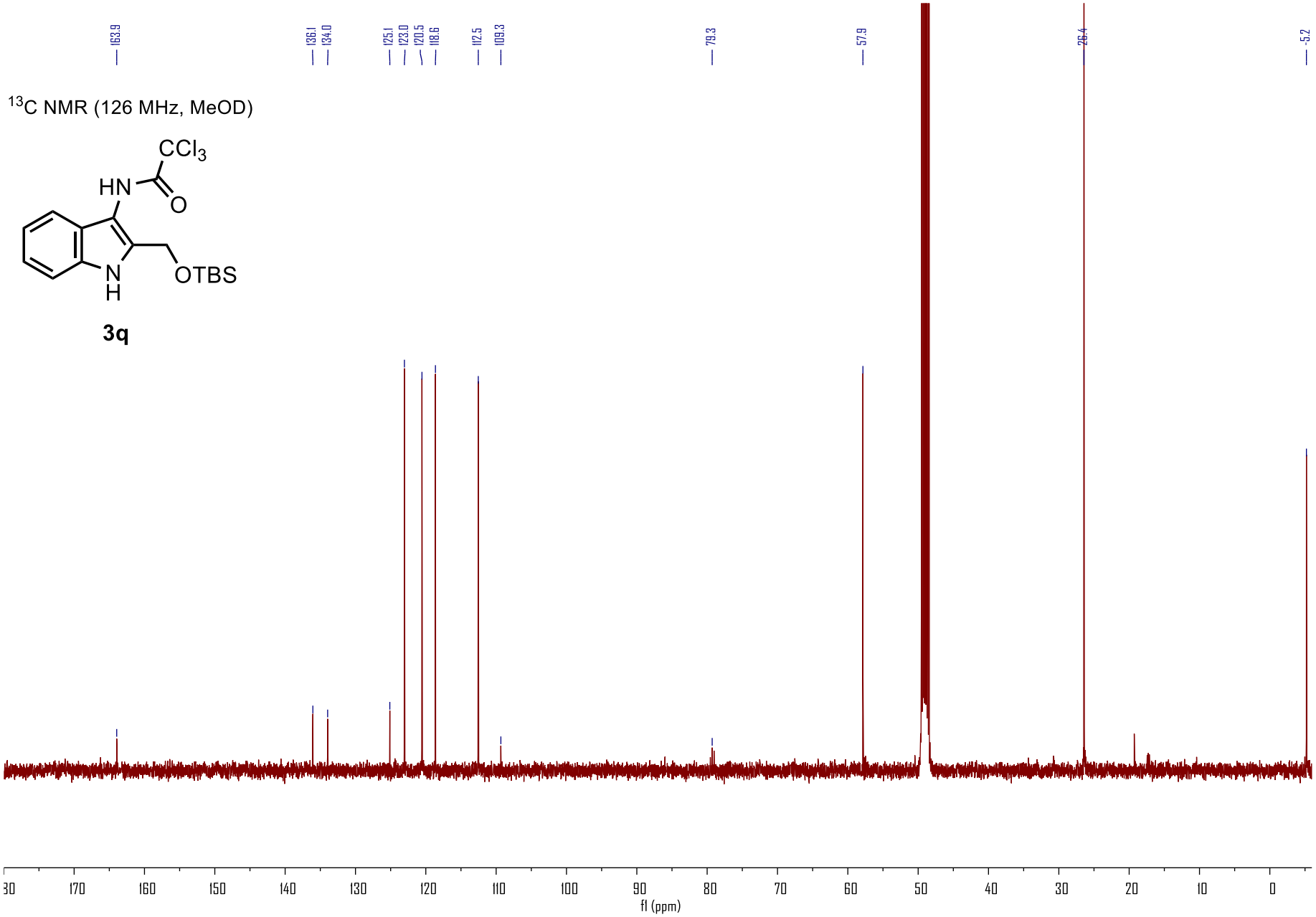

7.78
7.54
7.39
7.38
7.29
7.28
7.25
7.24
7.23
7.22
7.18
7.17
7.15
7.14
7.12
7.11
3.05
3.04
3.03
3.02
3.01
3.00
2.98
2.98
1H NMR (500 MHz, CDCl3)
CCl3
HN
O
N
H
3p
1.00
1.06
1.22
1.63
2.19
1.58
3.54
4.63
f1 (ppm)

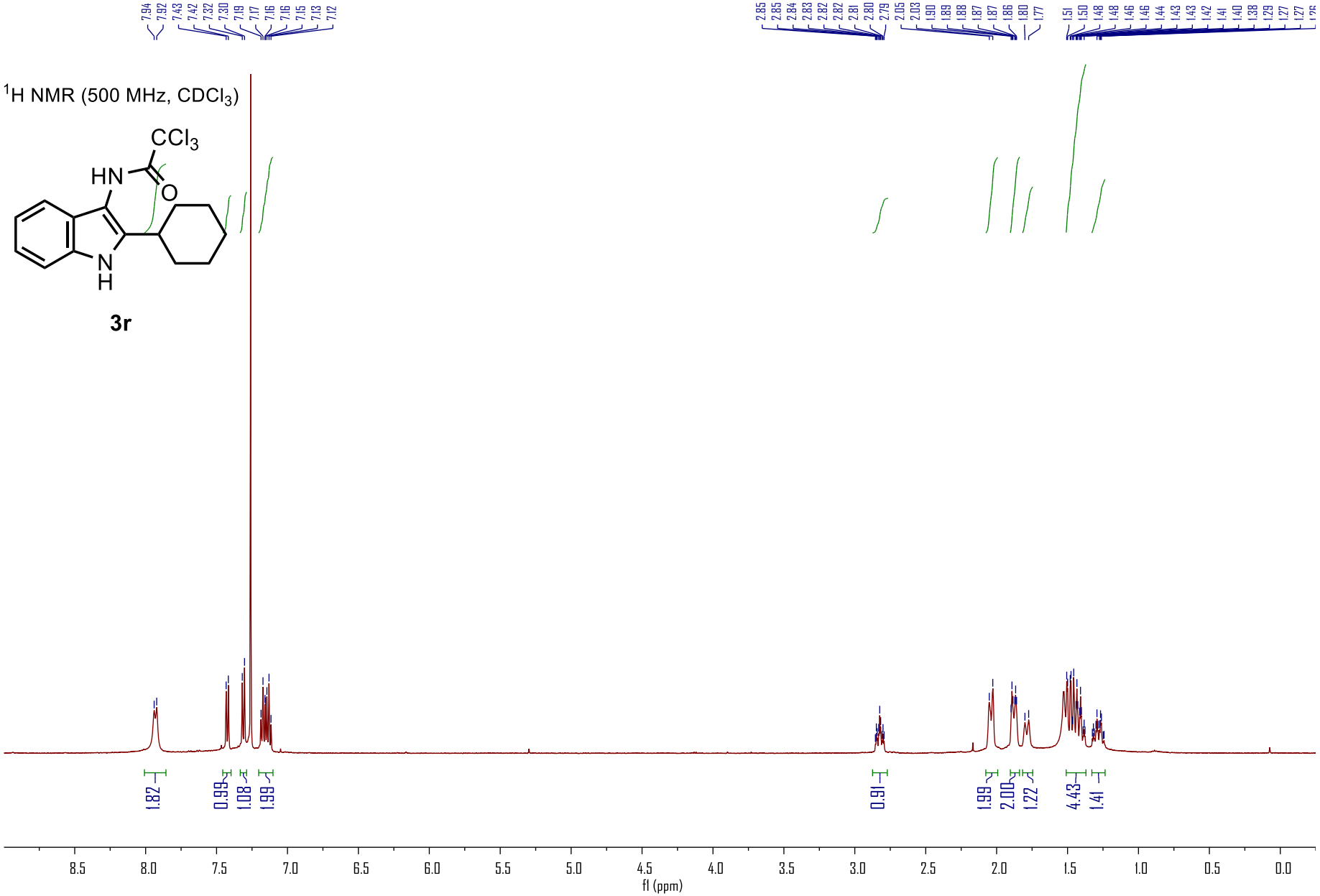

161.5
140.8
134.1
133.9
128.9
128.7
126.8
124.3
122.5
120.6
117.4
111.1
108.7
92.9
35.3
28.2
^{13}C NMR (126 MHz, $CDCl_3$)
CCl_3
HN
O
N
H
3p
f1 (ppm)

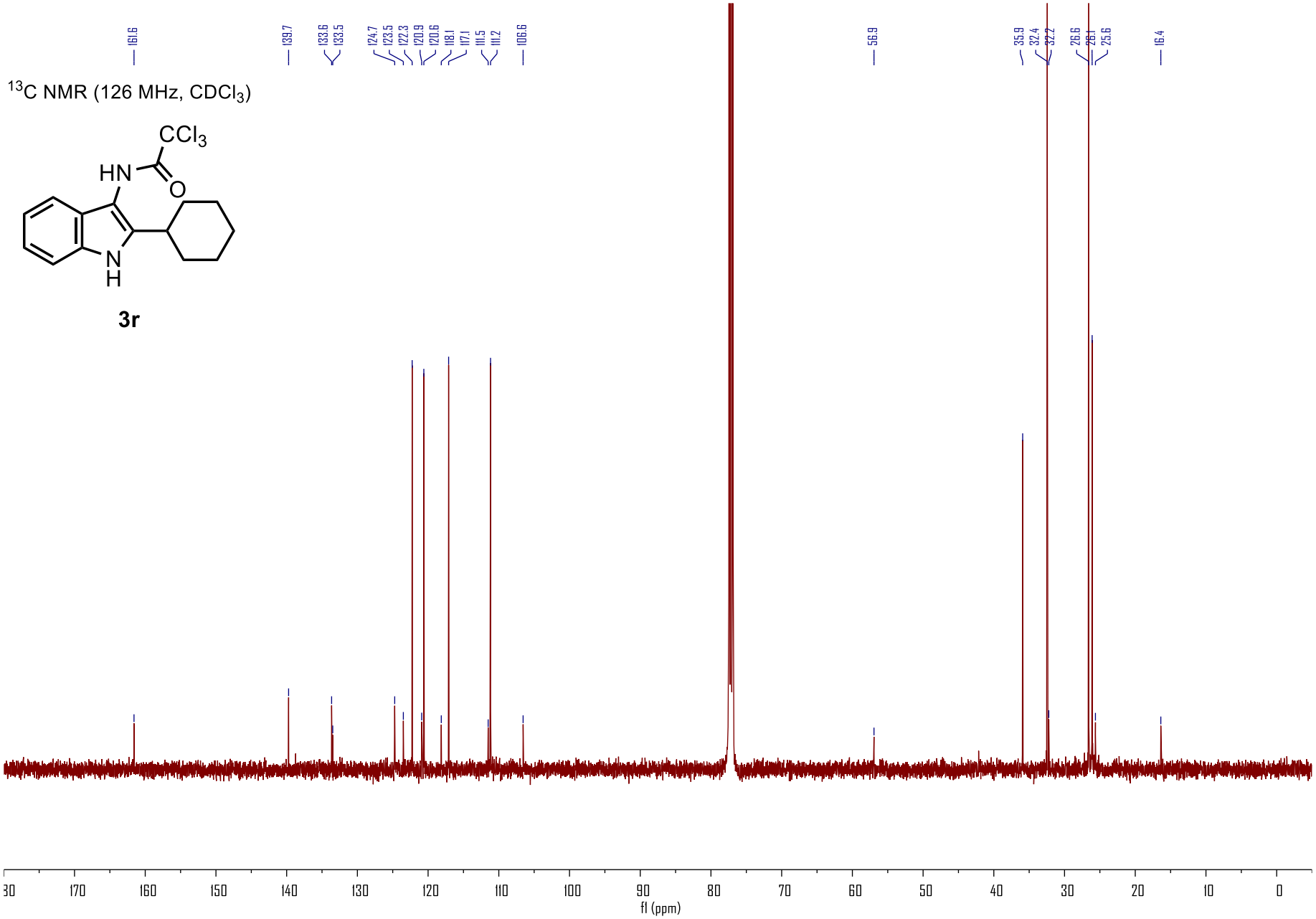
^{1}H NMR (500 MHz, MeOD)

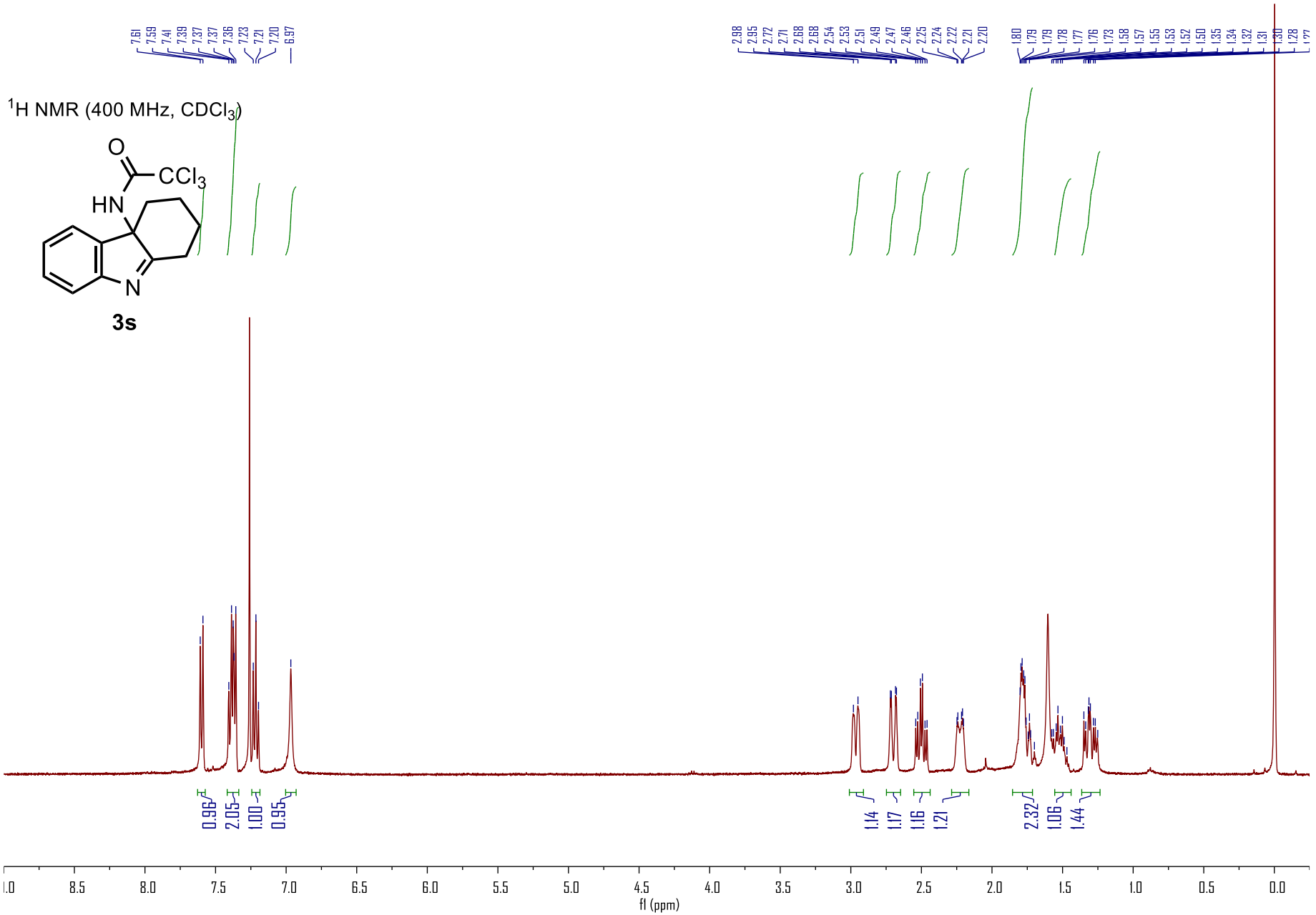


3q

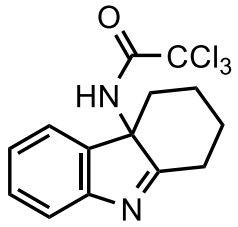

163.9
136.1
134.0
125.1
123.0
120.5
118.6
112.5
109.3
79.3
57.9
26.4
-5.2
^{13}C NMR (126 MHz, MeOD)
CCl3
HN
O
N
H
OTBS
3q
f1 (ppm)


^{1}H NMR (500 MHz, $CDCl_3$)
CCl_3
HN
O
N
H
3r
fl (ppm)


161.6
139.7
133.6
133.5
124.7
123.5
122.3
120.9
120.6
118.1
117.1
111.5
111.2
106.6
56.9
35.9
32.4
32.2
26.6
26.1
25.6
16.4
^{13}C NMR (126 MHz, $CDCl_3$)
CCl_3
HN
O
N
H
3r
f1 (ppm)

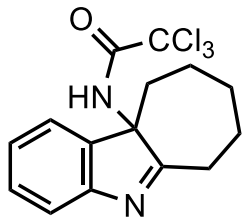

1H NMR (400 MHz, CDCl3)
O
CCl3
HN
N
3s
7.61
7.59
7.41
7.39
7.37
7.37
7.36
7.23
7.21
7.20
6.97
2.98
2.95
2.72
2.71
2.68
2.68
2.54
2.53
2.51
2.49
2.47
2.46
2.25
2.24
2.22
2.21
2.20
1.80
1.79
1.79
1.78
1.77
1.76
1.73
1.58
1.57
1.55
1.53
1.52
1.50
1.35
1.34
1.32
1.31
1.30
1.28
0.96
2.05
1.00
0.95
1.14
1.17
1.16
1.21
2.32
1.06
1.44
f1 (ppm)

^{13}C NMR (101 MHz, $CDCl_3$)



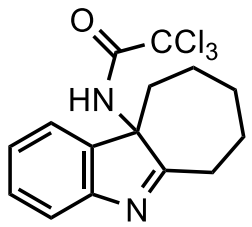
3s

^{1}H NMR (400 MHz, $CDCl_3$)



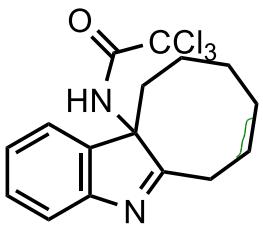
3t

^{13}C NMR (101 MHz, $CDCl_3$)

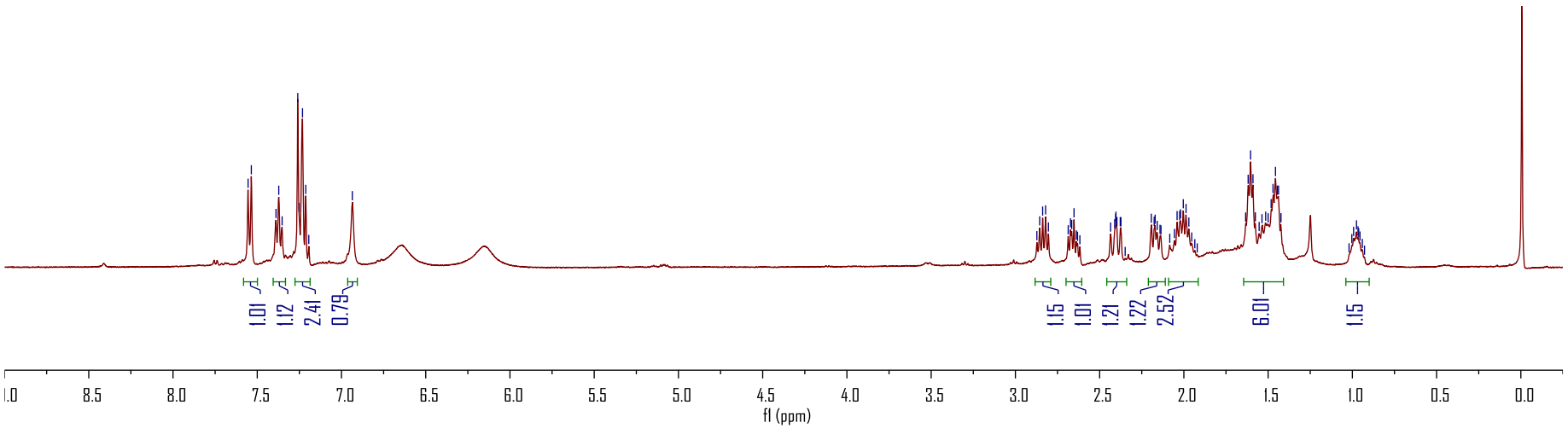


3t

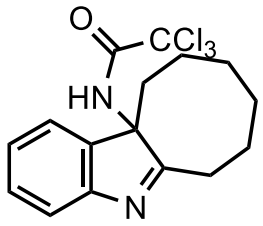
^{1}H NMR (400 MHz, $CDCl_3$)



3u

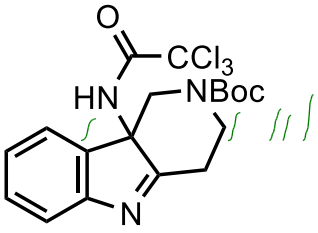


^{13}C NMR (101 MHz, $CDCl_3$)

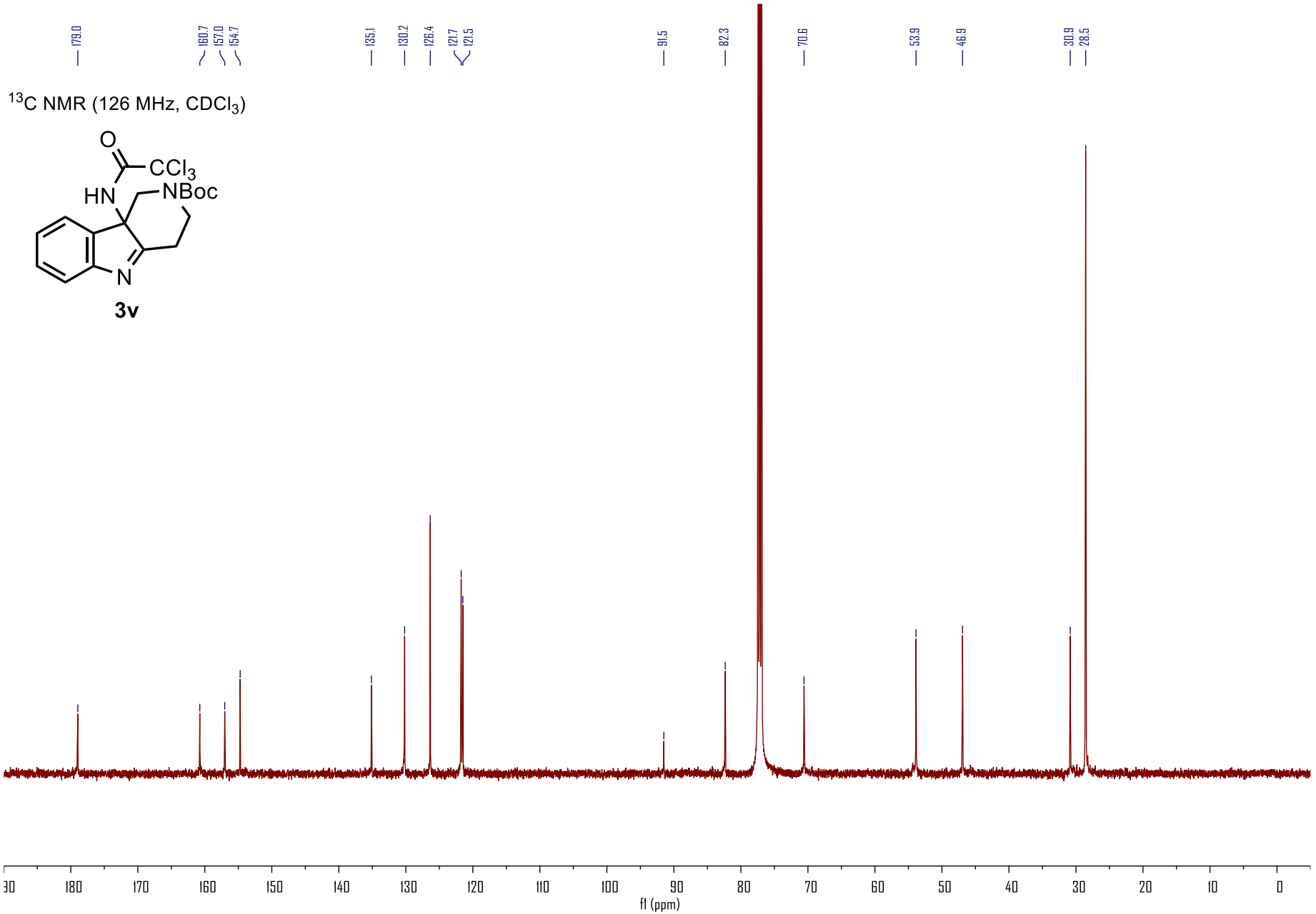


3u

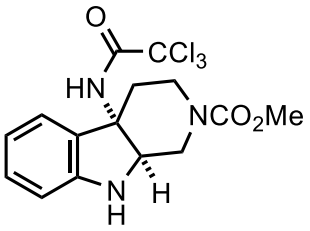
^{1}H NMR (500 MHz, $CDCl_3$)



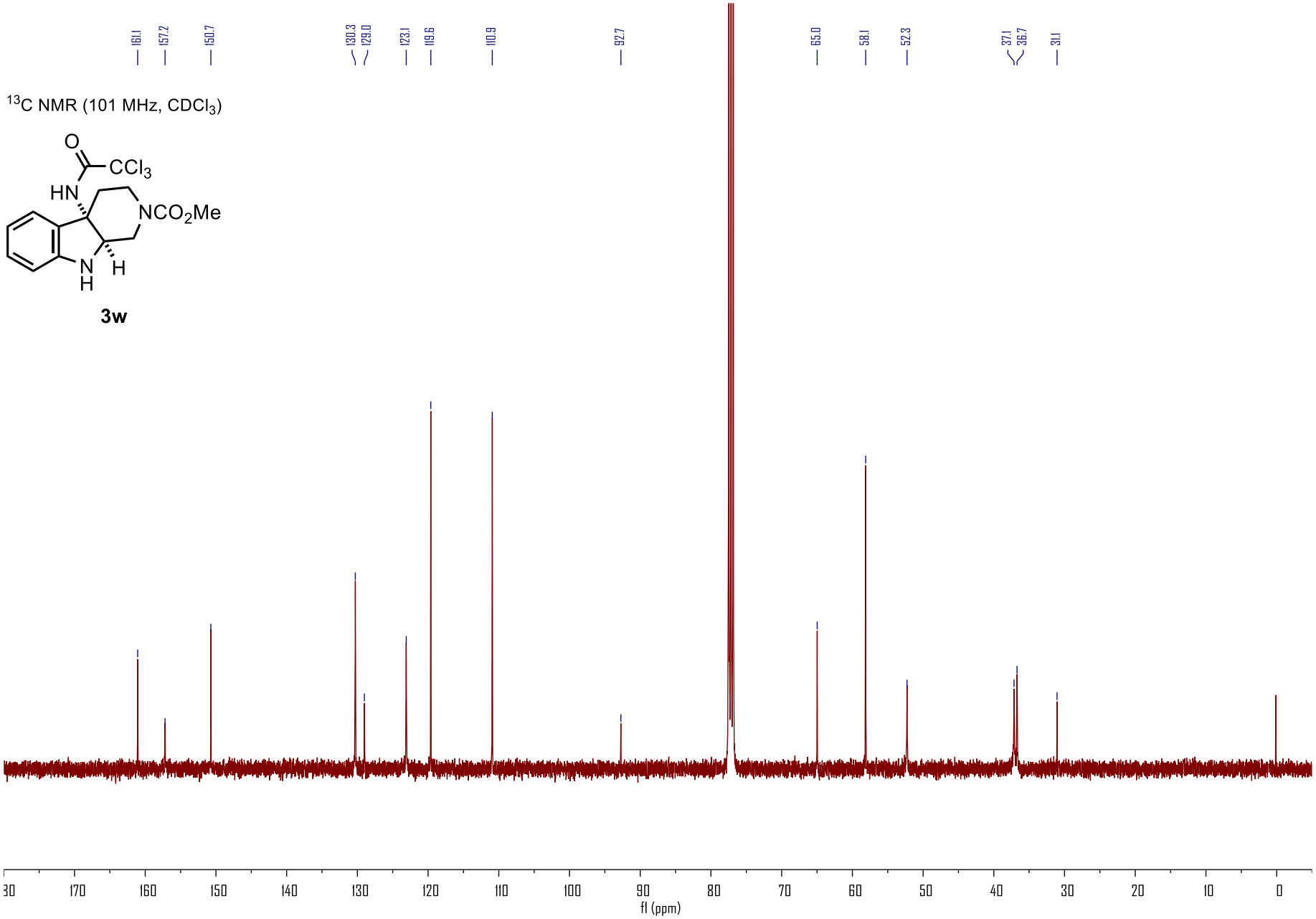
3v

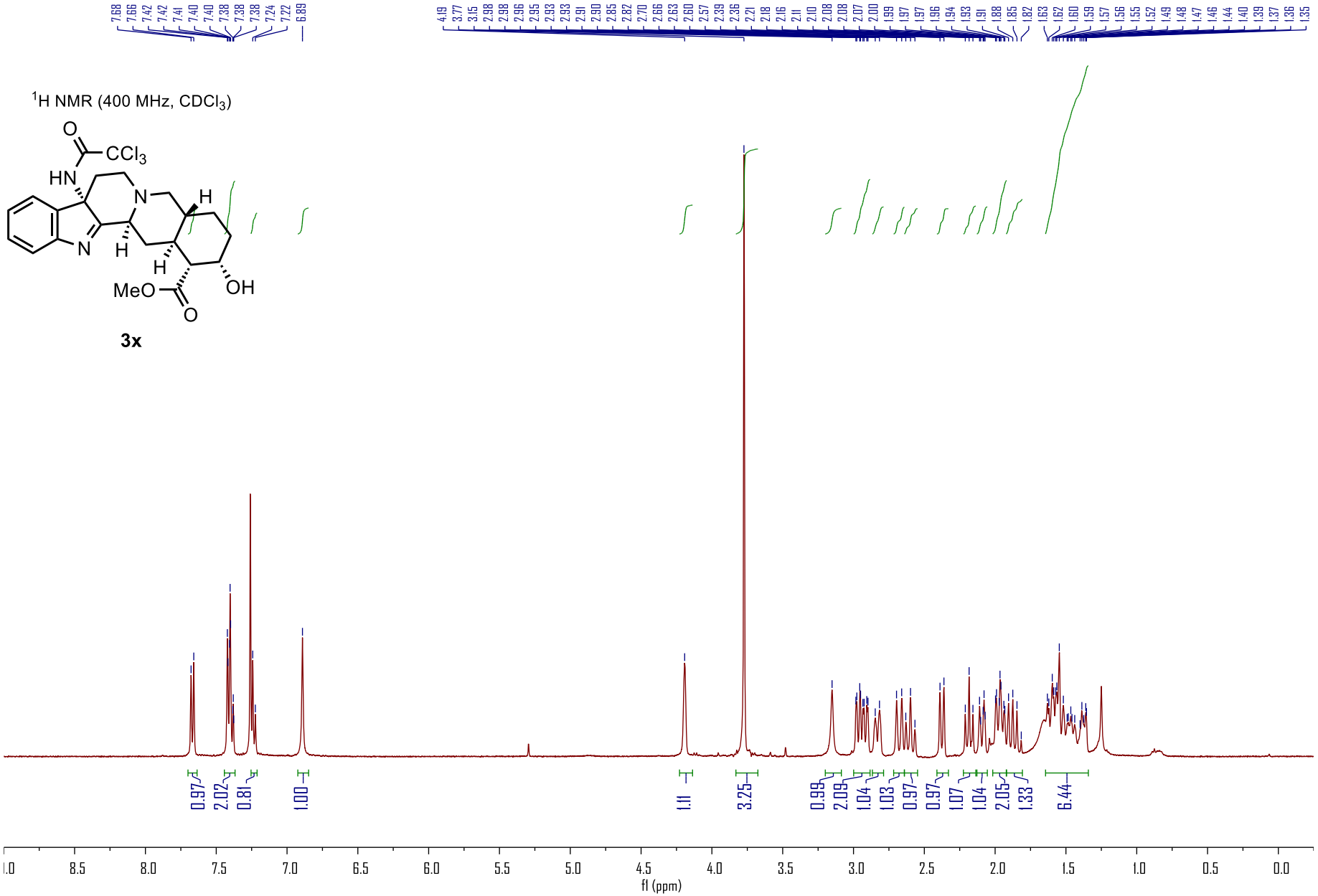

179.0
160.7
157.0
154.7
135.1
130.2
126.4
121.7
121.5
91.5
82.3
70.6
53.9
46.9
30.9
28.5
^{13}C NMR (126 MHz, $CDCl_3$)
O
CCl_3
HN
NBoc
N
3v
f1 (ppm)

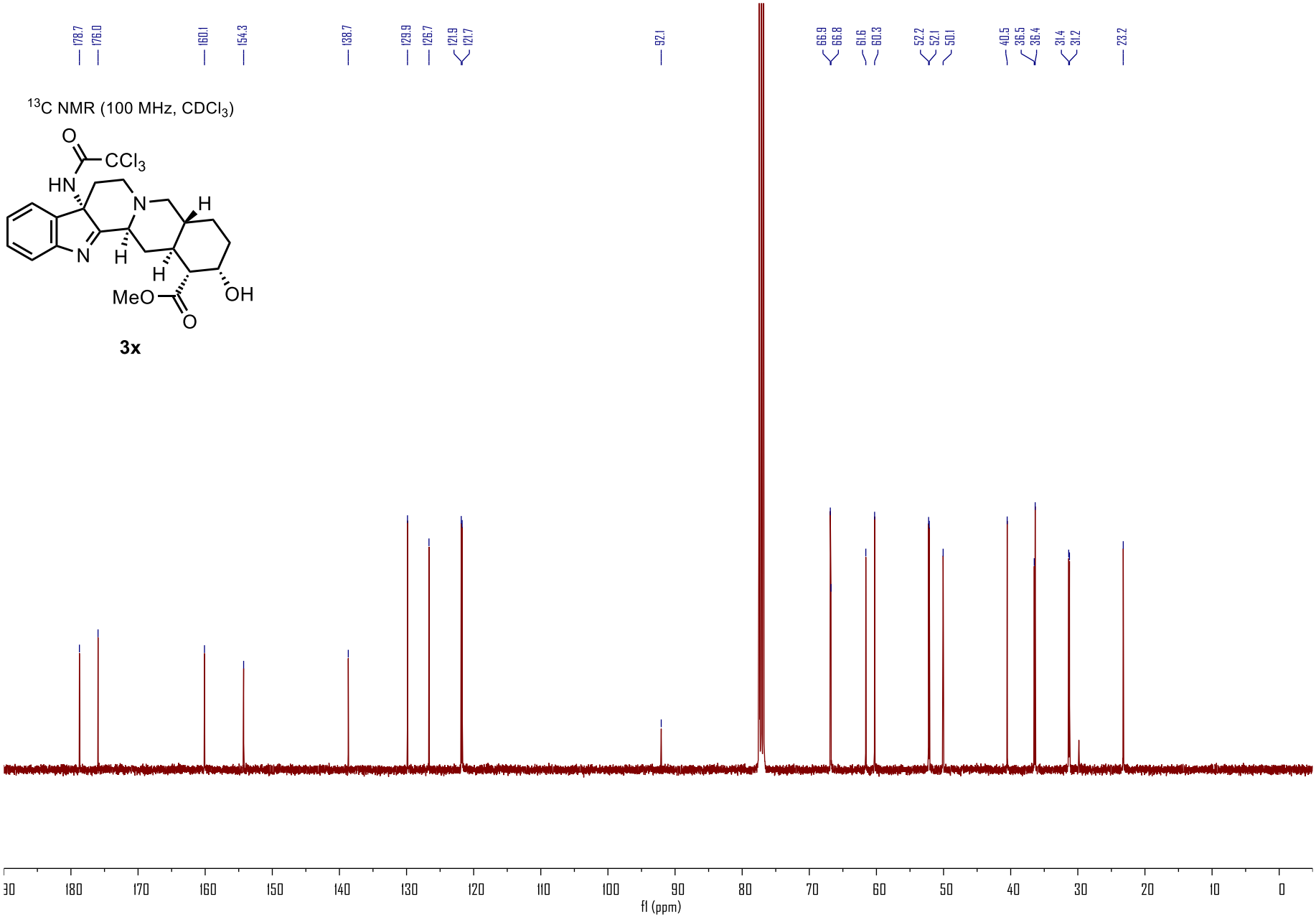
^{1}H NMR (400 MHz, $CDCl_3$)



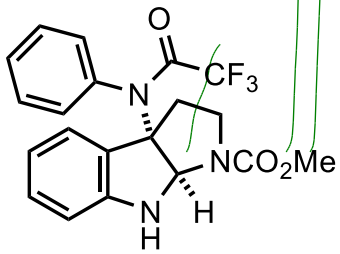
3w


161.1
157.2
150.7
130.3
129.0
123.1
119.6
110.9
92.7
65.0
58.1
52.3
37.1
36.7
31.1
^{13}C NMR (101 MHz, $CDCl_3$)
O
CCl_3
HN
NCO_2Me
N
H
H
3w
f1 (ppm)

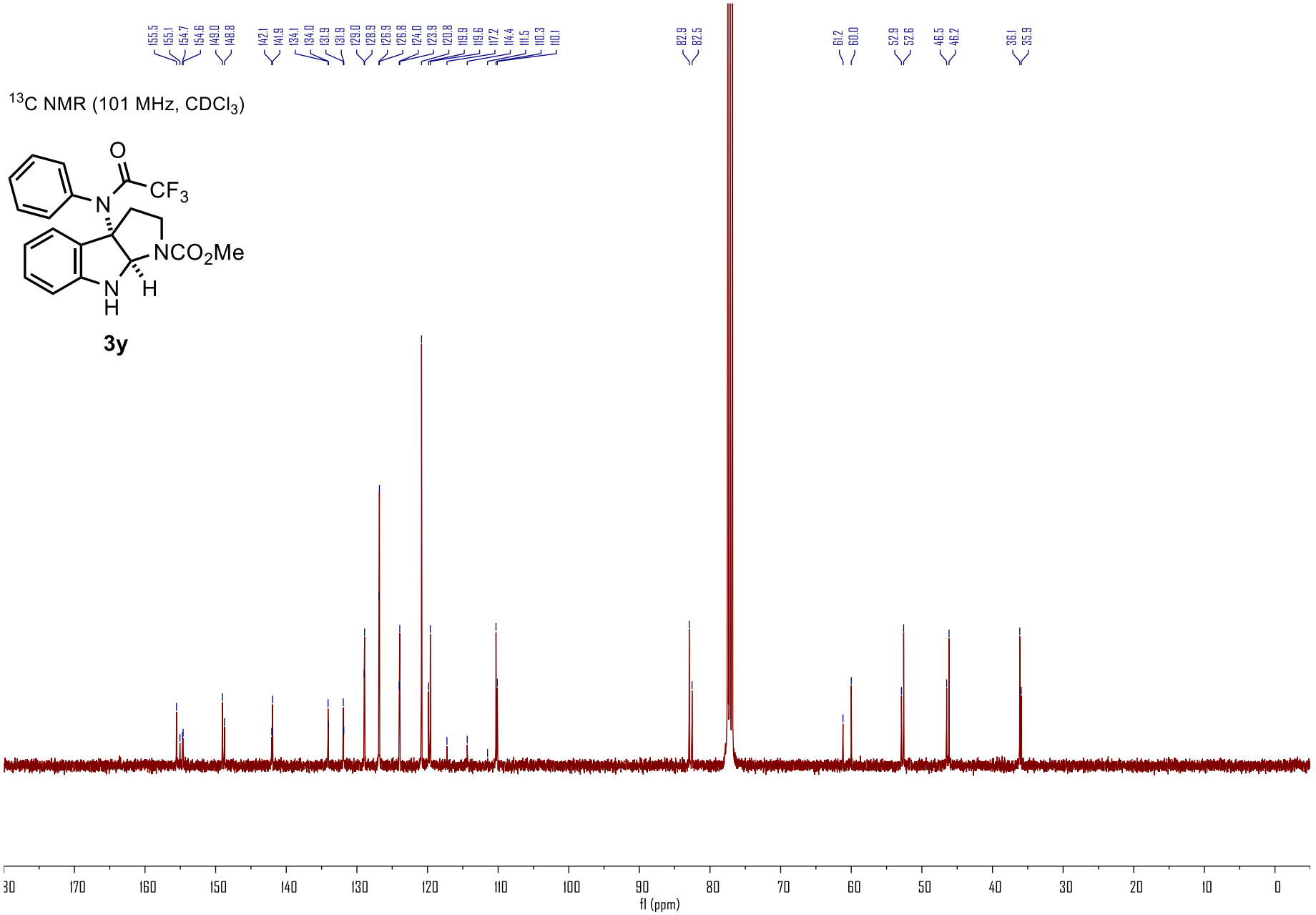

7.68
7.66
7.42
7.42
7.41
7.40
7.40
7.38
7.38
7.38
7.24
7.22
6.89
4.19
3.77
3.15
2.98
2.98
2.96
2.95
2.93
2.93
2.91
2.90
2.85
2.82
2.70
2.66
2.63
2.60
2.57
2.39
2.36
2.21
2.18
2.16
2.11
2.10
2.08
2.08
2.07
2.00
1.99
1.97
1.97
1.96
1.94
1.93
1.91
1.88
1.85
1.82
1.63
1.62
1.60
1.59
1.57
1.56
1.55
1.52
1.49
1.48
1.47
1.46
1.44
1.40
1.39
1.37
1.36
1.35
^{1}H NMR (400 MHz, $CDCl_3$)
O
CCl_3
HN
N
H
N
H
H
MeO
O
OH
3x
0.97
2.02
0.81
1.00
1.11
3.25
0.99
2.09
1.04
1.03
0.97
0.97
1.07
1.04
2.05
1.33
6.44
f1 (ppm)


178.7
176.0
160.1
154.3
138.7
129.9
126.7
121.9
121.7
92.1
66.9
66.8
61.6
60.3
52.2
52.1
50.1
40.5
36.5
36.4
31.4
31.2
23.2
^{13}C NMR (100 MHz, $CDCl_3$)
O
CCl_3
HN
N
H
N
H
H
MeO
O
OH
3x
f1 (ppm)

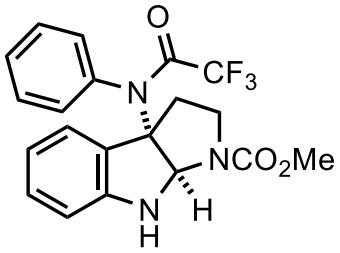
^{1}H NMR (400 MHz, $CDCl_3$)



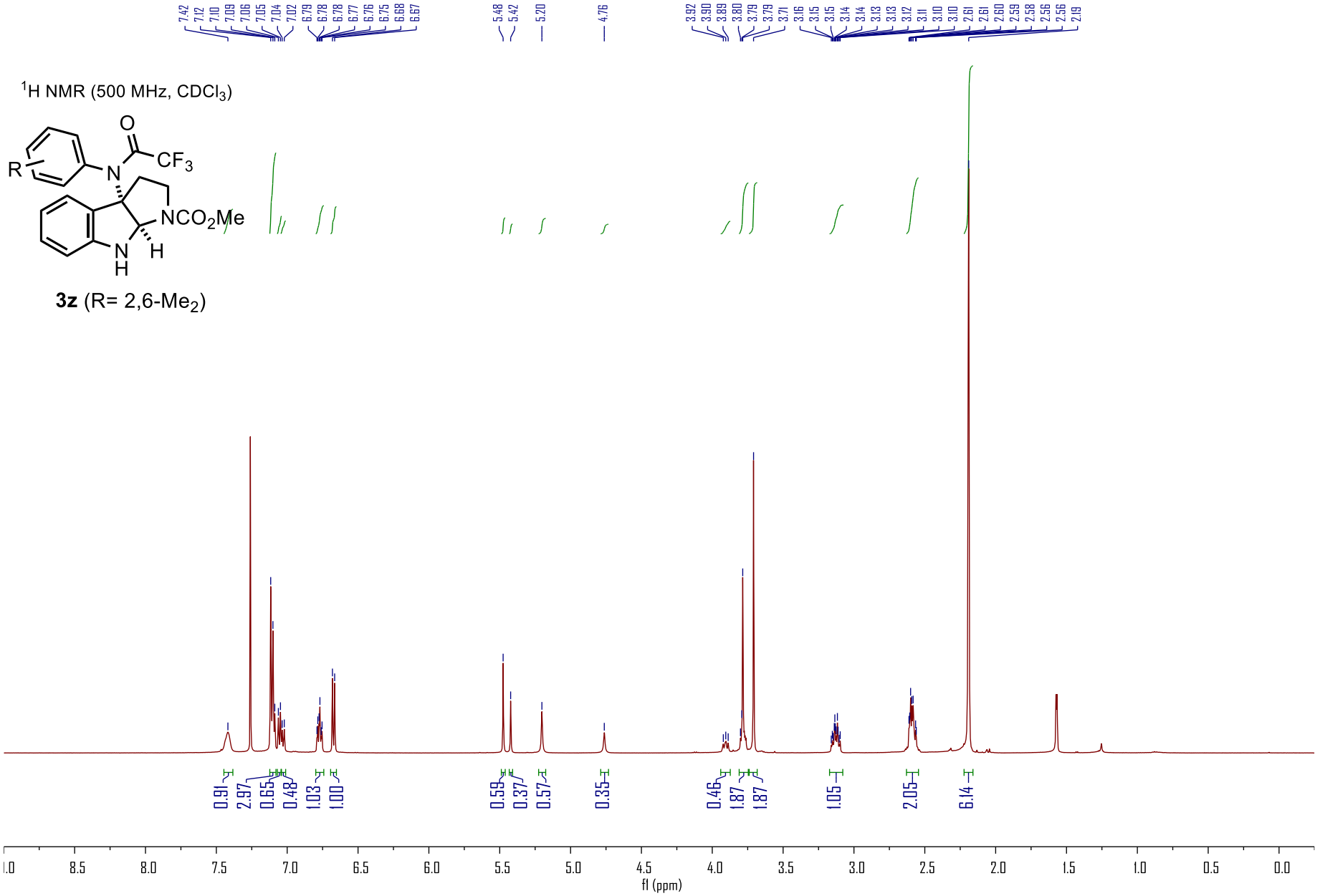
3y


155.5
155.1
154.7
154.6
149.0
148.8
142.1
141.9
134.1
134.0
131.9
131.9
129.0
128.9
126.9
126.8
124.0
123.9
120.8
119.9
119.6
117.2
114.4
111.5
110.3
110.1
82.9
82.5
61.2
60.0
52.9
52.6
46.5
46.2
36.1
35.9
^{13}C NMR (101 MHz, $CDCl_3$)
O
CF_3
N
NCO_2Me
N
H
H
3y
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)

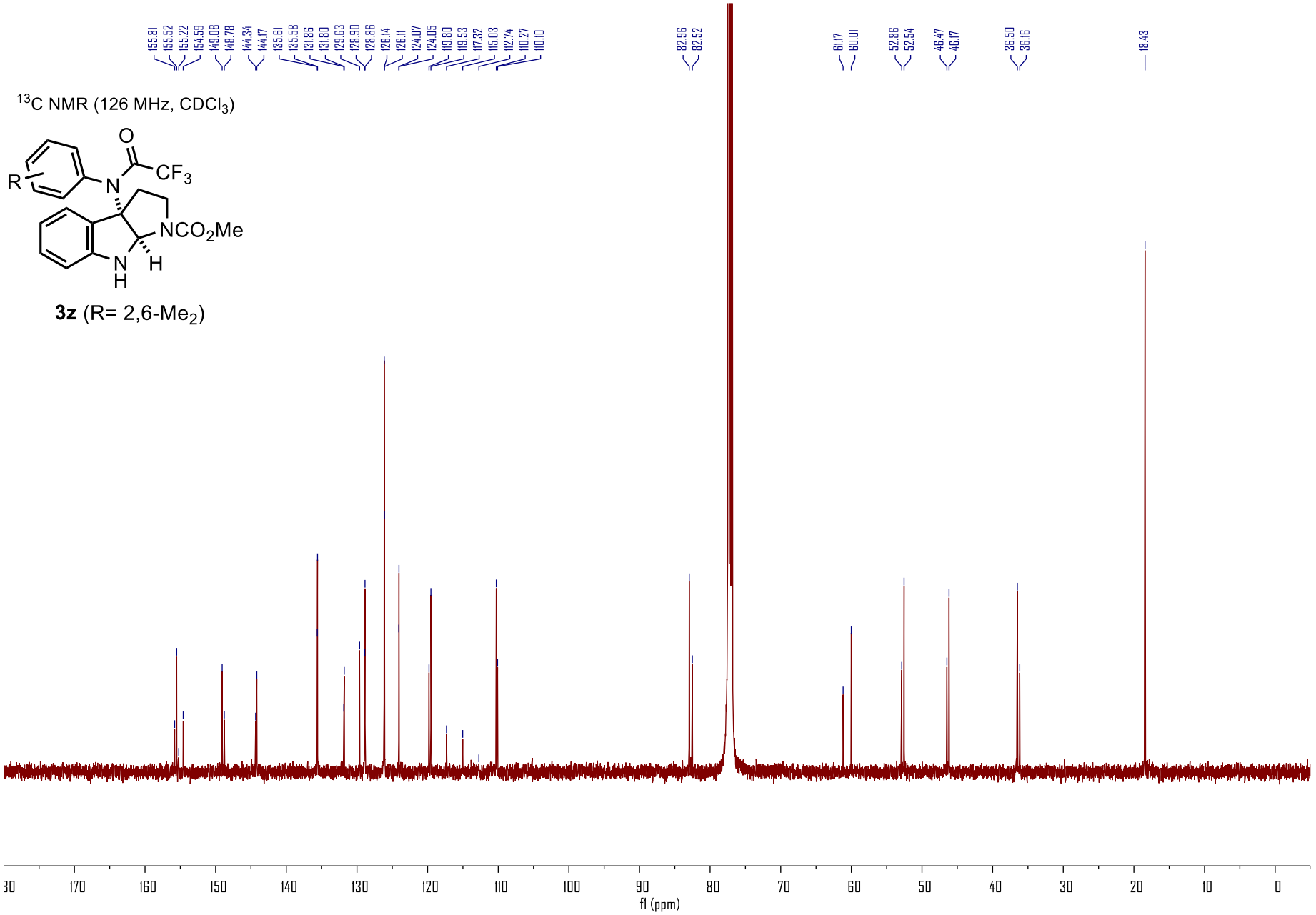


3y

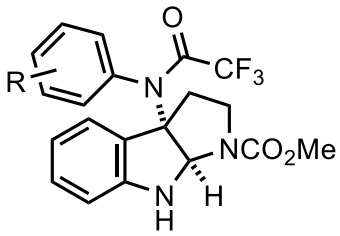


^{1}H NMR (500 MHz, $CDCl_3$)

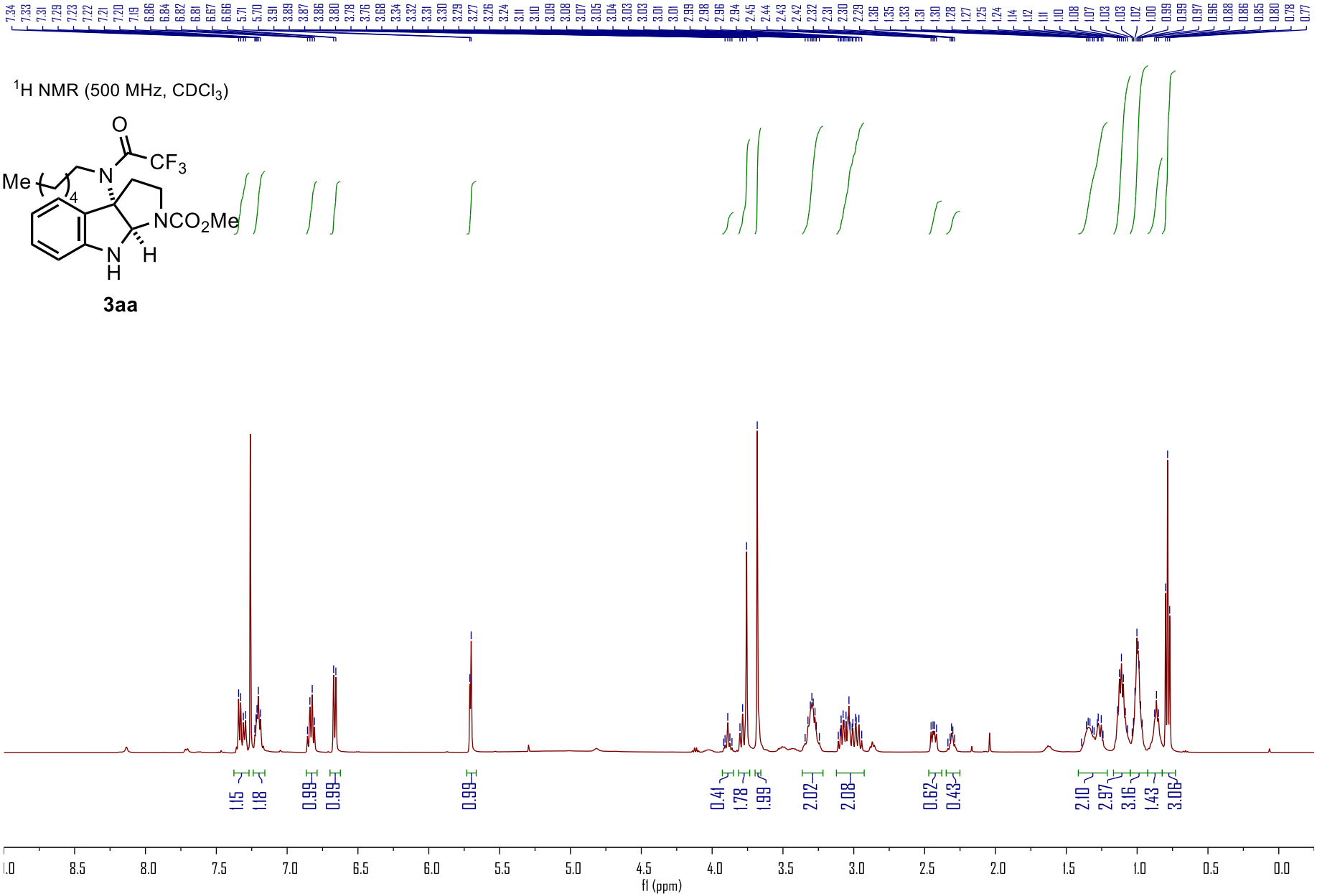
3z (R= 2,6-Me_2)

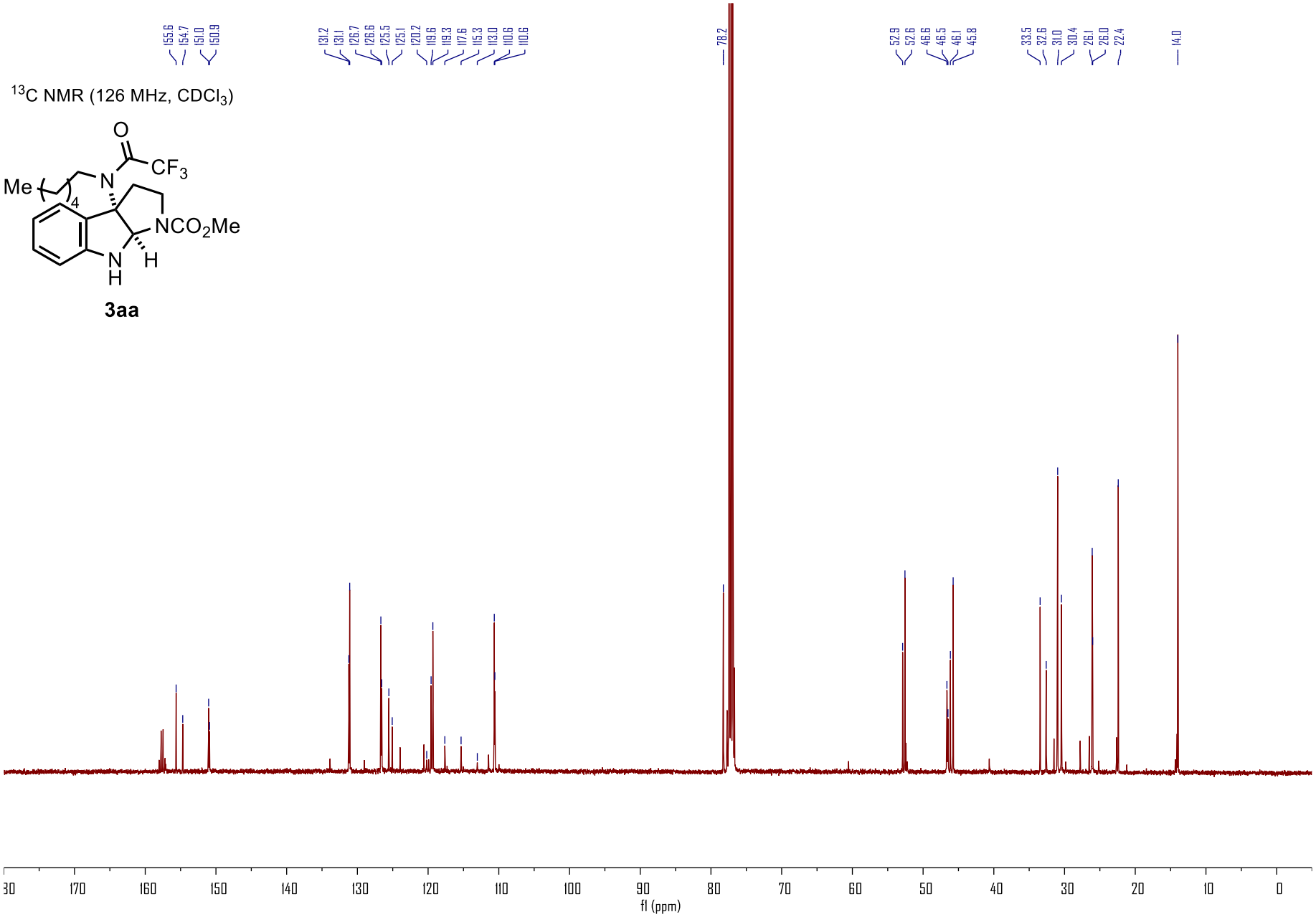

155.81
155.52
155.22
154.59
149.08
148.78
144.34
144.17
135.61
135.58
131.86
131.80
129.63
128.90
128.86
126.14
126.11
124.07
124.05
119.80
119.53
117.32
115.03
112.74
110.27
110.10
82.96
82.52
61.17
60.01
52.86
52.54
46.47
46.17
36.50
36.16
18.43
13C NMR (126 MHz, CDCl3)
O
CF3
R
N
NCO2Me
N
H
H
3z (R= 2,6-Me2)
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

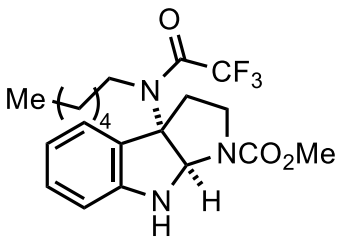


3z (R= 2,6-Me_2)

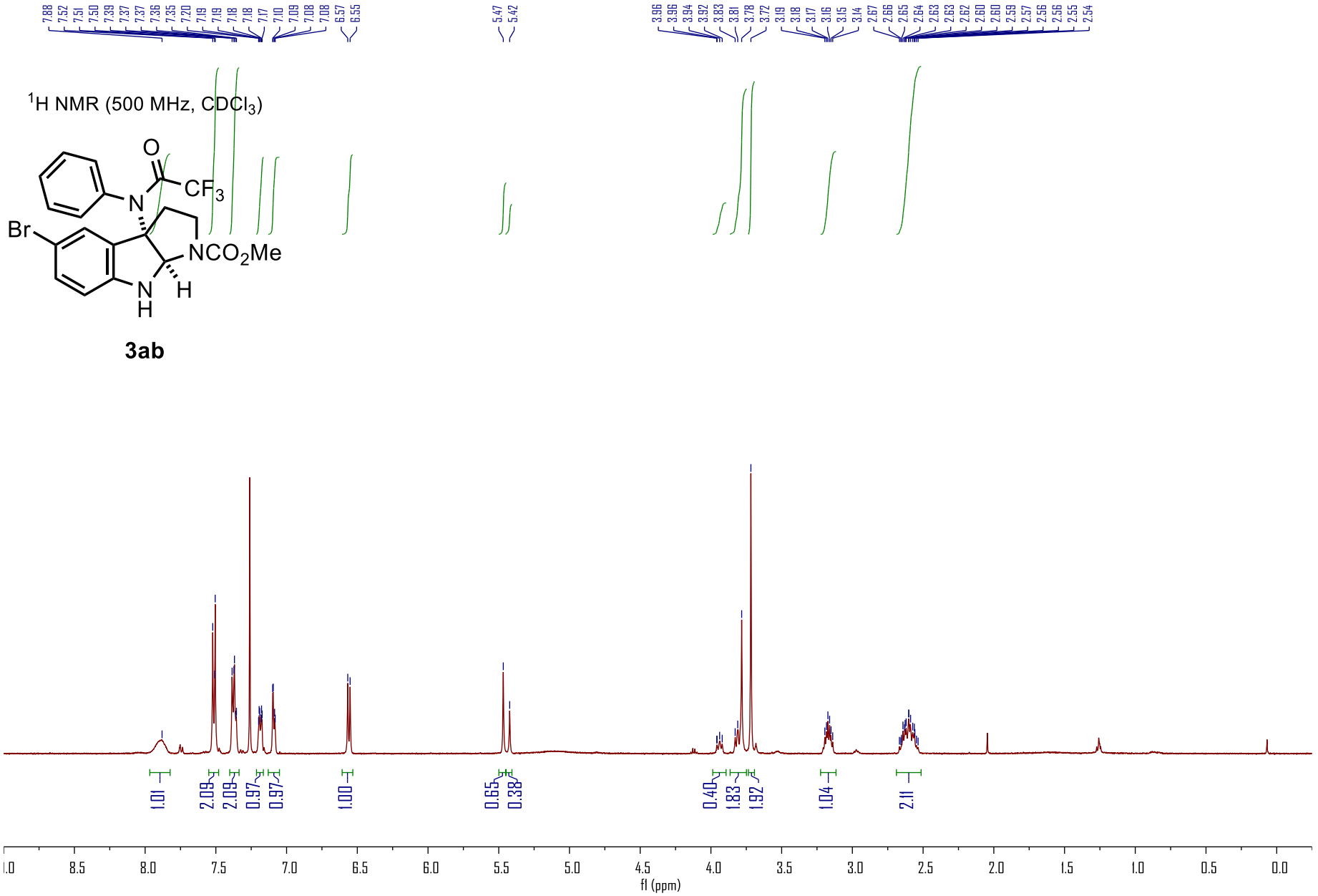

7.34 7.33 7.31 7.29 7.23 7.22 7.21 7.20 7.19 6.86 6.84 6.82 6.81 6.67 6.66 5.71 5.70 3.91 3.89 3.87 3.86 3.80 3.78 3.76 3.68 3.34 3.32 3.31 3.30 3.29 3.27 3.26 3.24 3.11 3.10 3.09 3.08 3.07 3.05 3.04 3.03 3.03 3.01 3.01 2.99 2.98 2.96 2.94 2.45 2.44 2.43 2.42 2.32 2.31 2.30 2.29 1.36 1.35 1.33 1.31 1.30 1.28 1.27 1.25 1.24 1.14 1.12 1.11 1.10 1.08 1.07 1.03 1.03 1.02 1.00 0.99 0.99 0.97 0.96 0.88 0.86 0.85 0.80 0.78 0.77
1H NMR (500 MHz, CDCl3)
O
CF3
N
Me
4
NCO2Me
N
H
H
3aa
1.15 1.18 0.99 0.99 0.99 0.41 1.78 1.99 2.02 2.08 0.62 0.43 2.10 2.97 3.16 1.43 3.06
f1 (ppm)

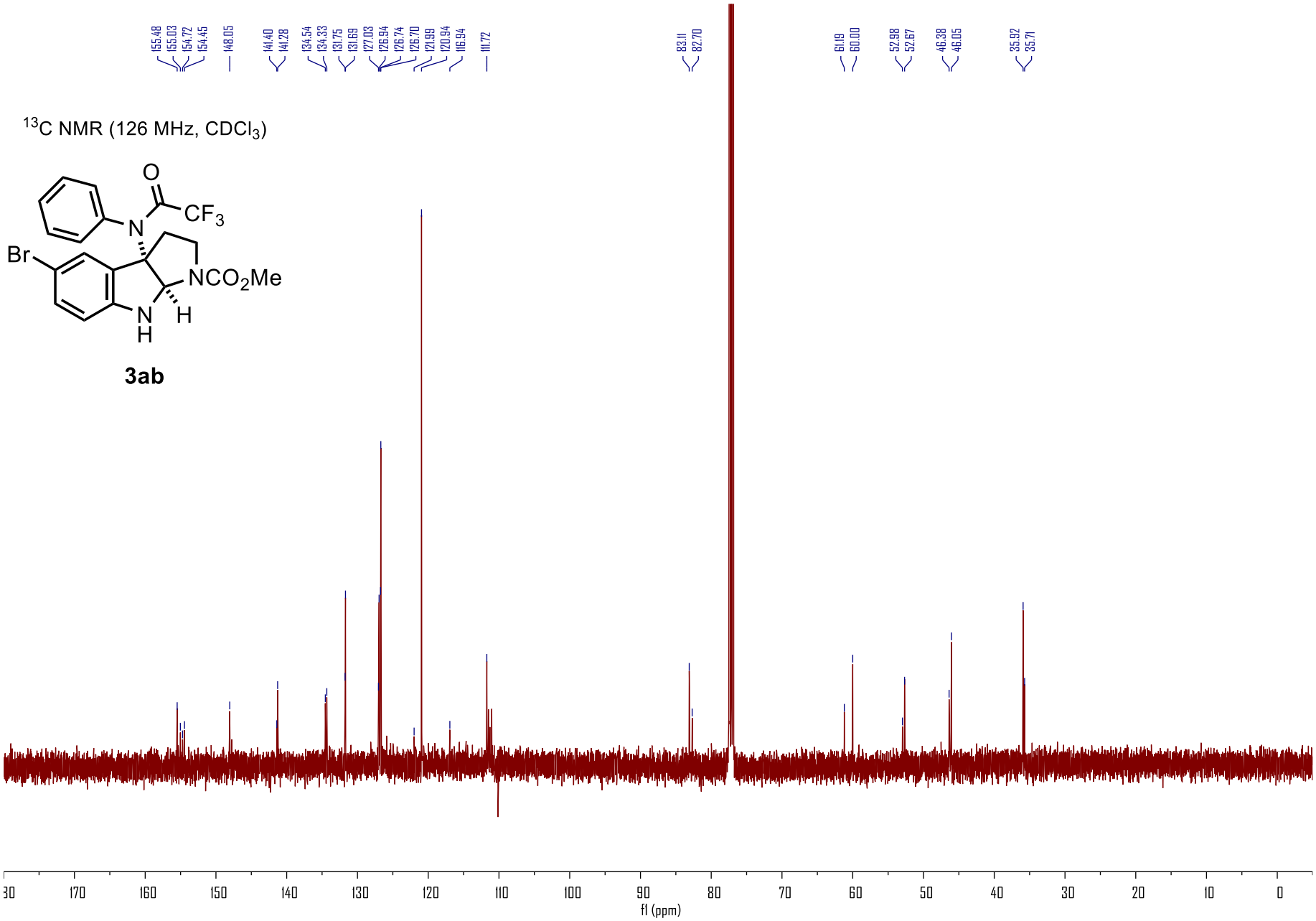

155.6
154.7
151.0
150.9
131.2
131.1
126.7
126.6
125.5
125.1
120.2
119.6
119.3
117.6
115.3
113.0
110.6
110.6
78.2
52.9
52.6
46.6
46.5
46.1
45.8
33.5
32.6
31.0
30.4
26.1
26.0
22.4
14.0
^{13}C NMR (126 MHz, $CDCl_3$)
O
CF_3
N
Me
4
NCO_2Me
N
H
H
3aa
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

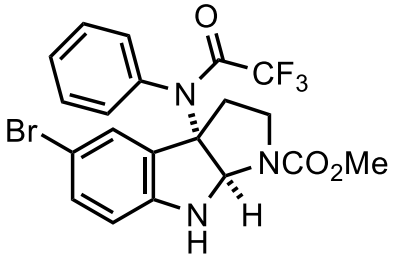


3aa

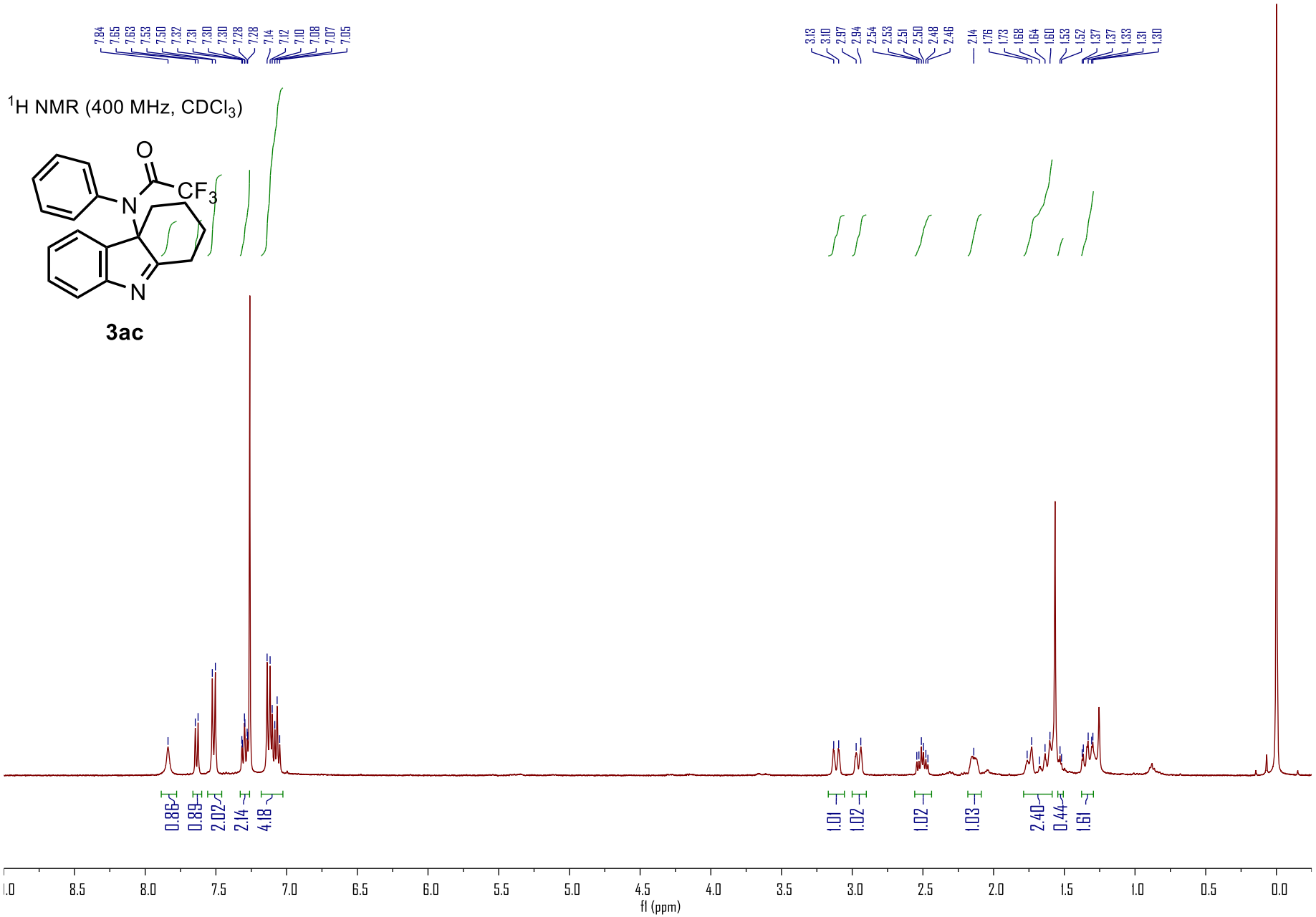

7.88
7.52
7.51
7.50
7.39
7.37
7.37
7.36
7.35
7.20
7.19
7.19
7.18
7.18
7.17
7.10
7.09
7.08
7.08
6.57
6.55
5.47
5.42
3.96
3.96
3.94
3.92
3.83
3.81
3.78
3.72
3.19
3.18
3.17
3.16
3.15
3.14
2.67
2.66
2.65
2.64
2.63
2.63
2.62
2.60
2.60
2.59
2.57
2.56
2.56
2.55
2.54
1H NMR (500 MHz, CDCl3)
O
CF3
N
Br
NCO2Me
N
H
H
3ab
1.01
2.08
2.09
0.97
0.97
1.00
0.65
0.38
0.40
1.83
1.92
1.04
2.11
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

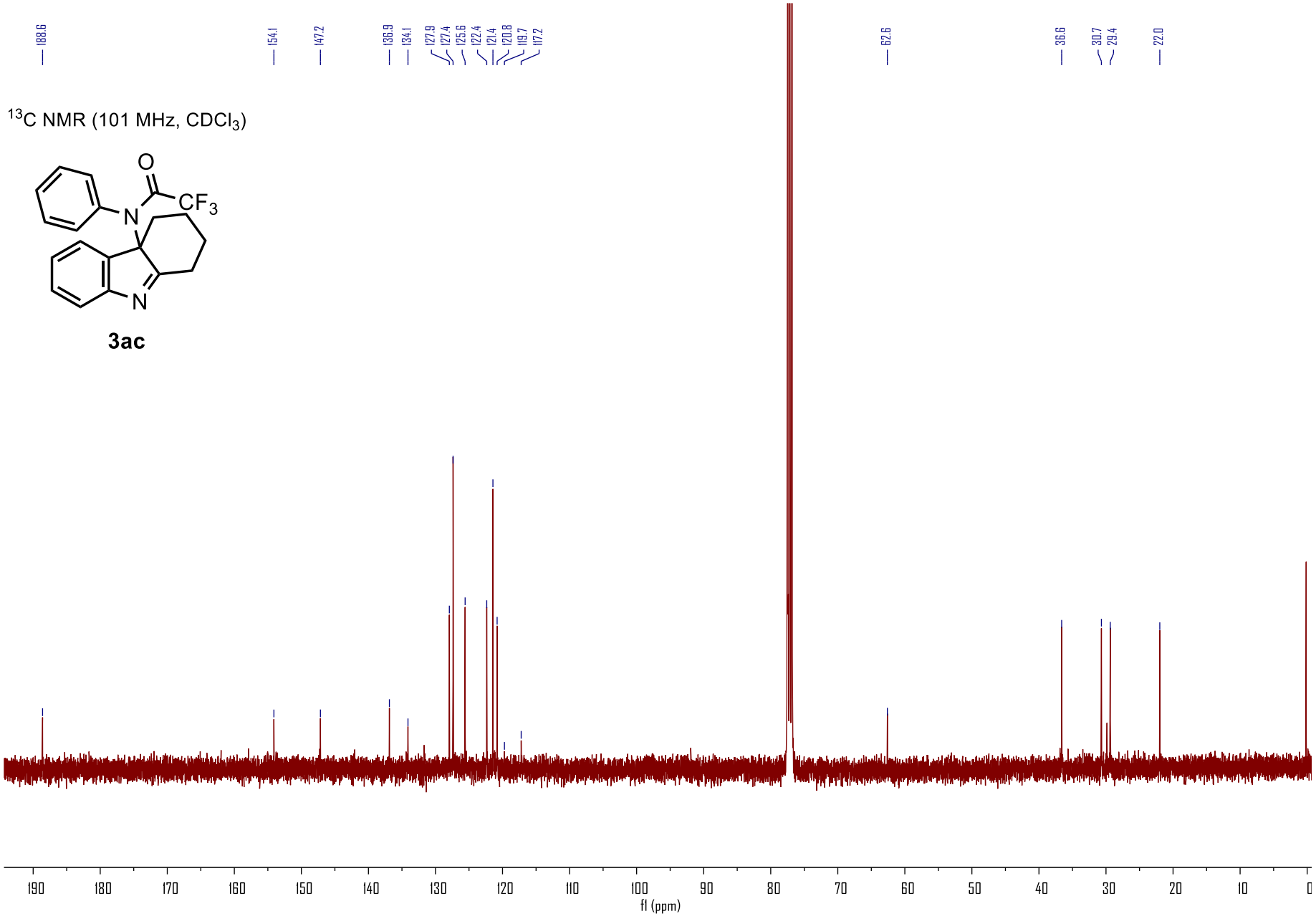

155.48
155.03
154.72
154.45
148.05
141.40
141.28
134.54
134.33
131.75
131.69
127.03
126.94
126.74
126.70
121.99
120.94
116.94
111.72
83.11
82.70
61.98
60.00
52.98
52.67
46.38
46.05
35.92
35.71
^{13}C NMR (126 MHz, $CDCl_3$)
O
CF_3
N
Br
NCO_2Me
N
H
H
3ab
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)

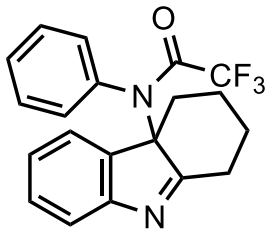


3ab

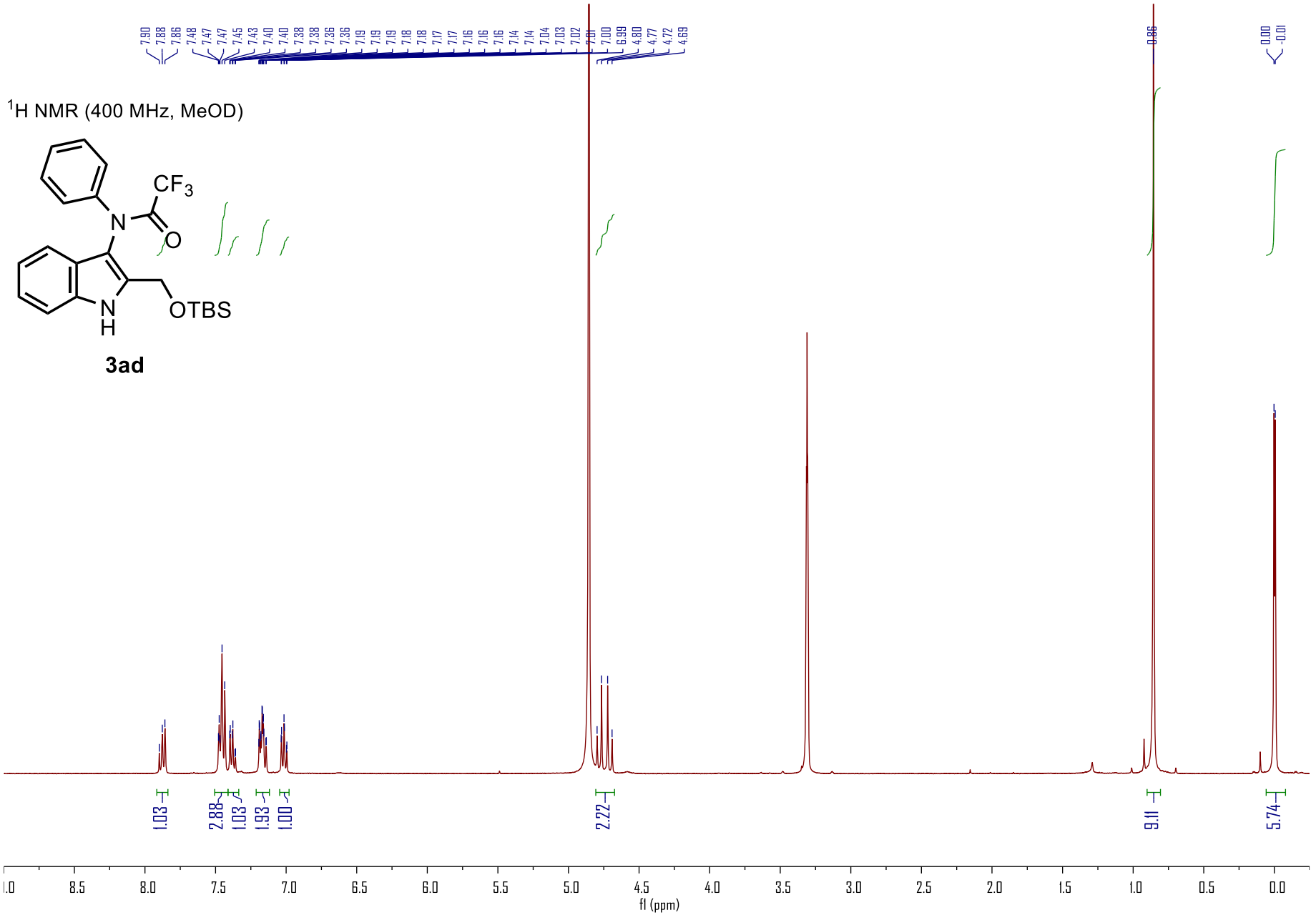

7.84
7.65
7.63
7.53
7.50
7.32
7.31
7.30
7.30
7.28
7.28
7.14
7.12
7.10
7.08
7.07
7.05
3.13
3.10
2.97
2.94
2.54
2.53
2.51
2.50
2.48
2.46
2.14
1.76
1.73
1.68
1.64
1.60
1.53
1.52
1.37
1.37
1.33
1.31
1.30
^{1}H NMR (400 MHz, $CDCl_3$)
O
CF_3
N
N
3ac
0.86
0.89
2.02
2.14
4.18
1.01
1.02
1.02
1.03
2.40
0.44
1.61
f1 (ppm)

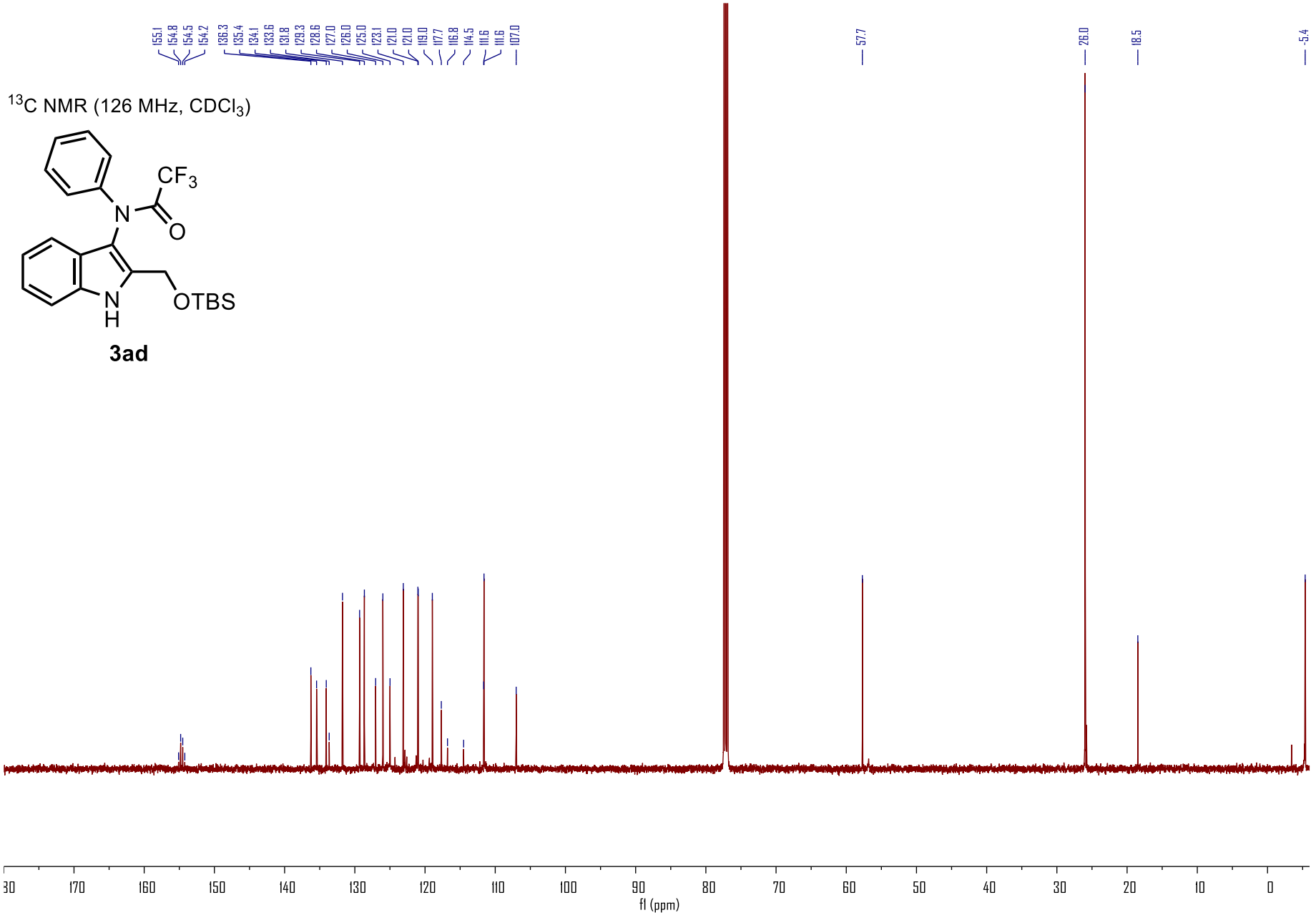

188.6
154.1
147.2
136.9
134.1
127.9
127.4
125.6
122.4
121.4
120.8
119.7
117.2
62.6
36.6
30.7
29.4
22.0
^{13}C NMR (101 MHz, $CDCl_3$)
O
CF_3
N
N
3ac
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)

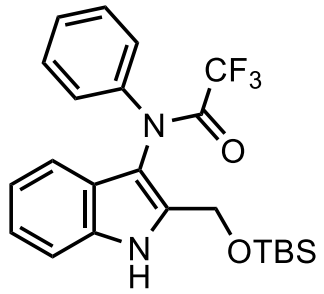


3ac


^{1}H NMR (400 MHz, MeOD)
CF3
N
O
N
H
OTBS
3ad
7.90
7.88
7.86
7.48
7.47
7.47
7.45
7.43
7.40
7.40
7.38
7.38
7.36
7.36
7.19
7.19
7.19
7.18
7.18
7.17
7.17
7.16
7.16
7.16
7.14
7.14
7.04
7.03
7.02
7.01
7.00
6.99
4.80
4.77
4.72
4.69
0.98
0.00
-0.01
1.03
2.88
1.03
1.93
1.00
2.22
9.11
5.74
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

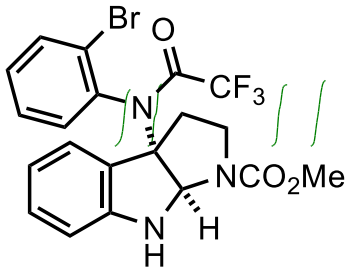

155.1
154.8
154.5
154.2
136.3
135.4
134.1
133.6
131.8
129.3
128.6
127.0
126.0
125.0
123.1
121.0
121.0
119.0
117.7
116.8
114.5
111.6
111.6
107.0
57.7
26.0
18.5
-5.4
13C NMR (126 MHz, CDCl3)
CF3
N
O
N
H
OTBS
3ad
f1 (ppm)

^{19}F NMR (376 MHz, MeOD)

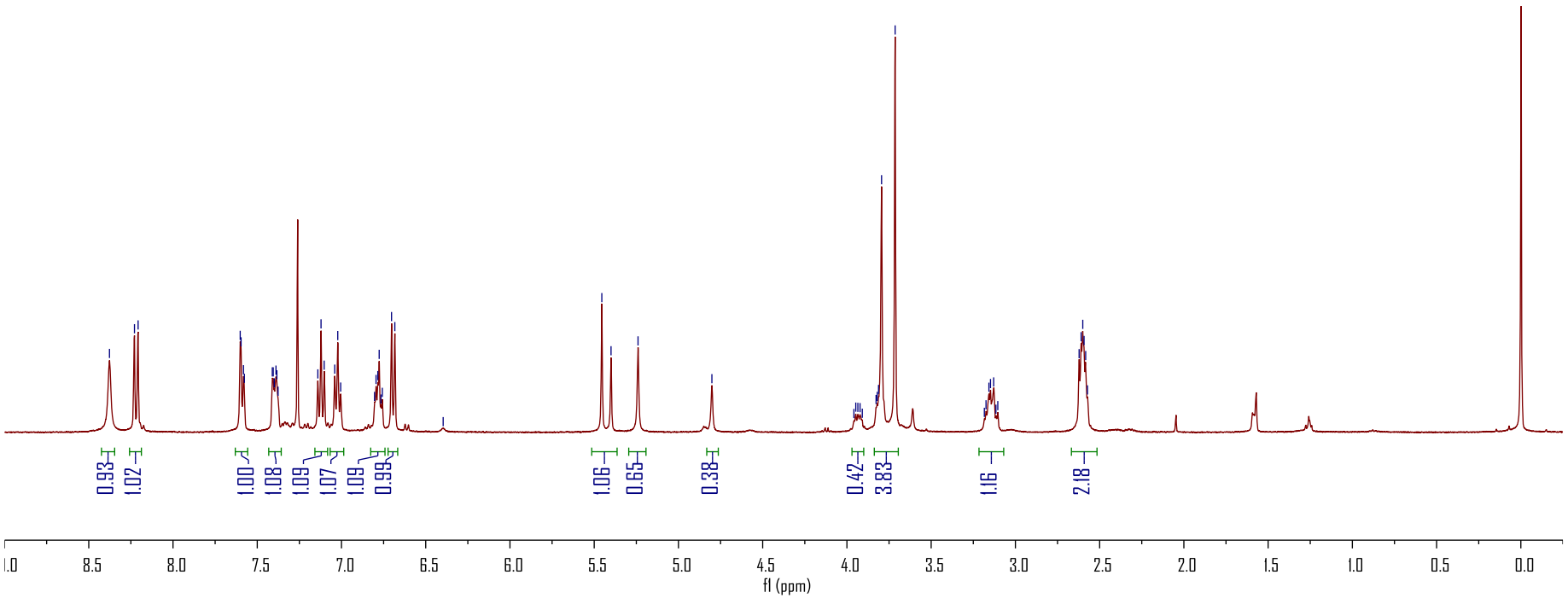


3ad

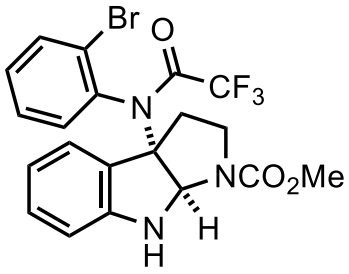
^{1}H NMR (400 MHz, $CDCl_3$)



3ae

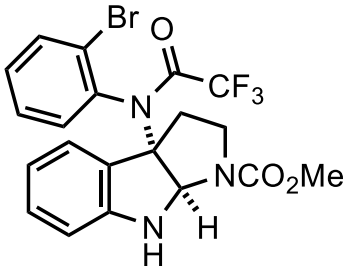


^{13}C NMR (101 MHz, $CDCl_3$)



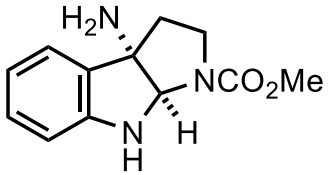
3ae

^{19}F NMR (471 MHz, $CDCl_3$)

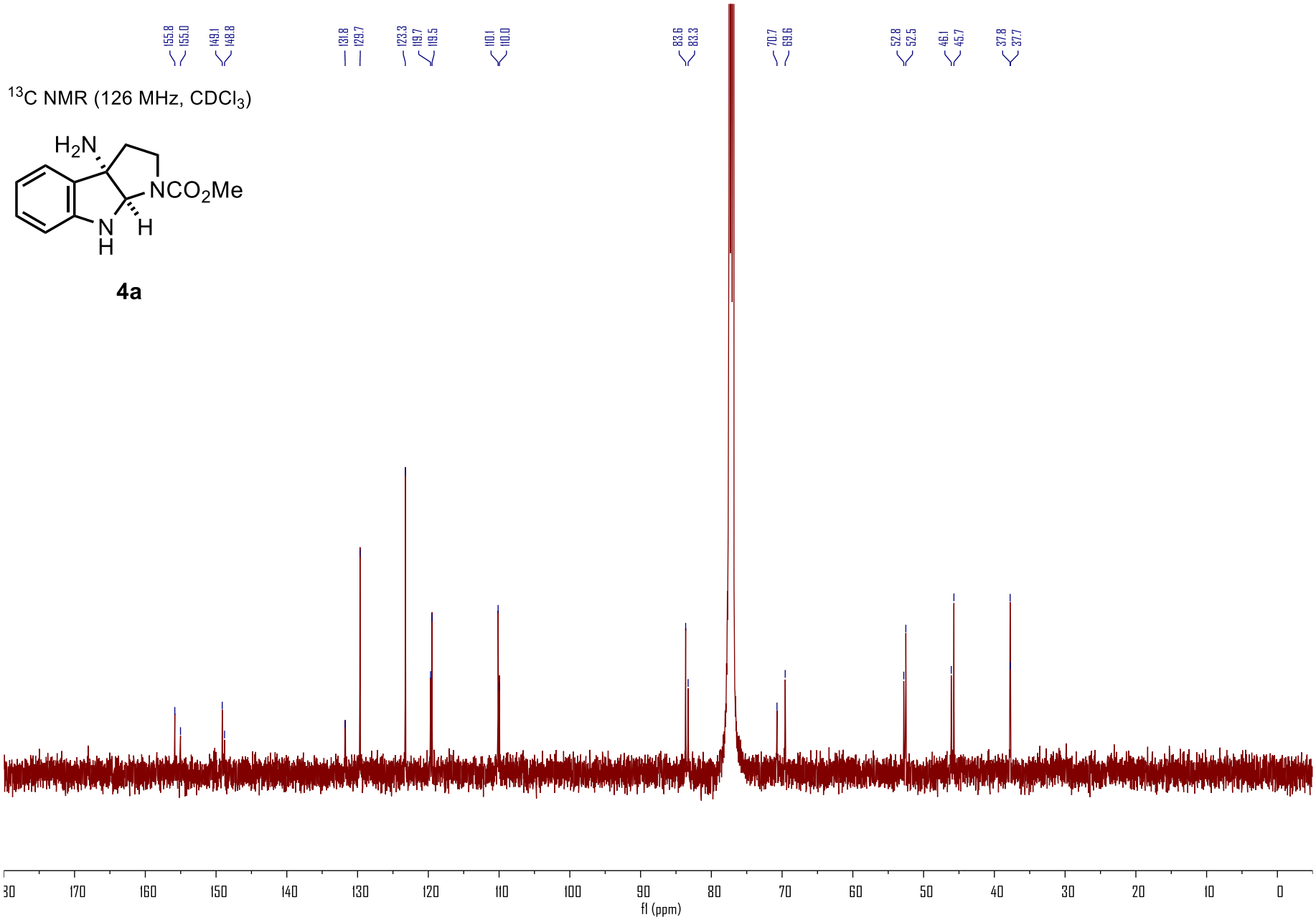


3ae

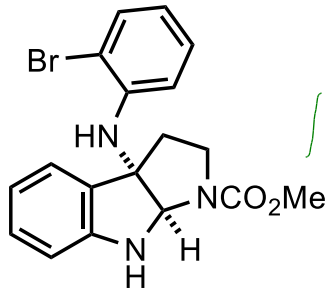
^{1}H NMR (500 MHz, $CDCl_3$)



4a

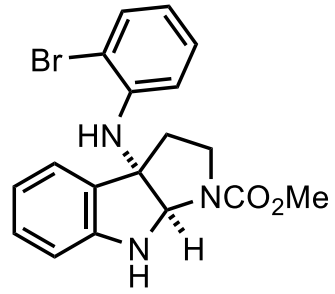

155.8
155.0
149.1
148.8
131.8
129.7
123.3
119.7
119.5
110.1
110.0
83.6
83.3
70.7
69.6
52.8
52.5
46.1
45.7
37.8
37.7
^{13}C NMR (126 MHz, $CDCl_3$)
H_2N
NCO_2Me
N
H
H
4a
f1 (ppm)

^{1}H NMR (500 MHz, $CDCl_3$)

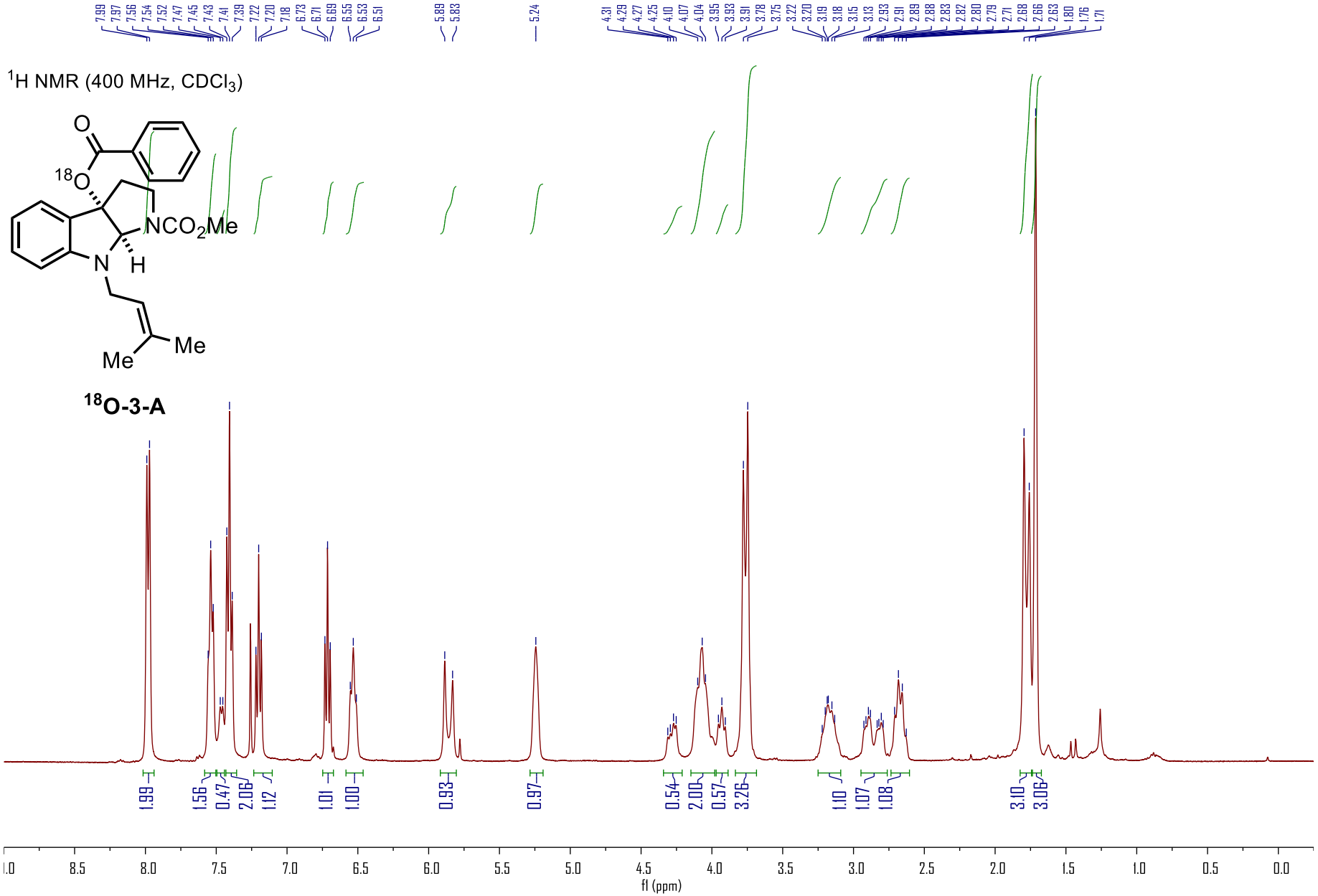


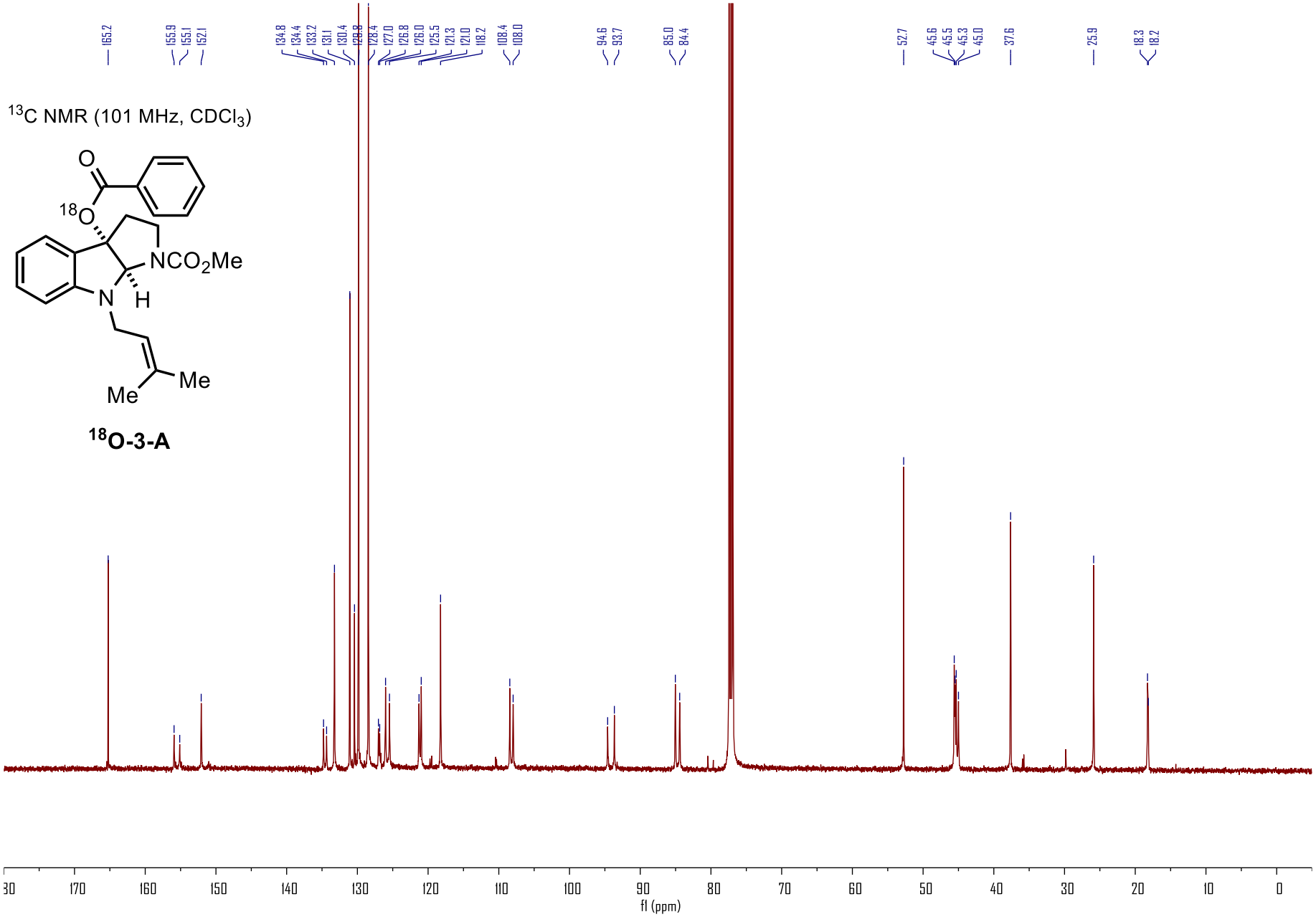
4ae

^{13}C NMR (126 MHz, $CDCl_3$)

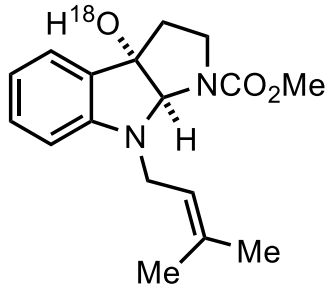


4ae

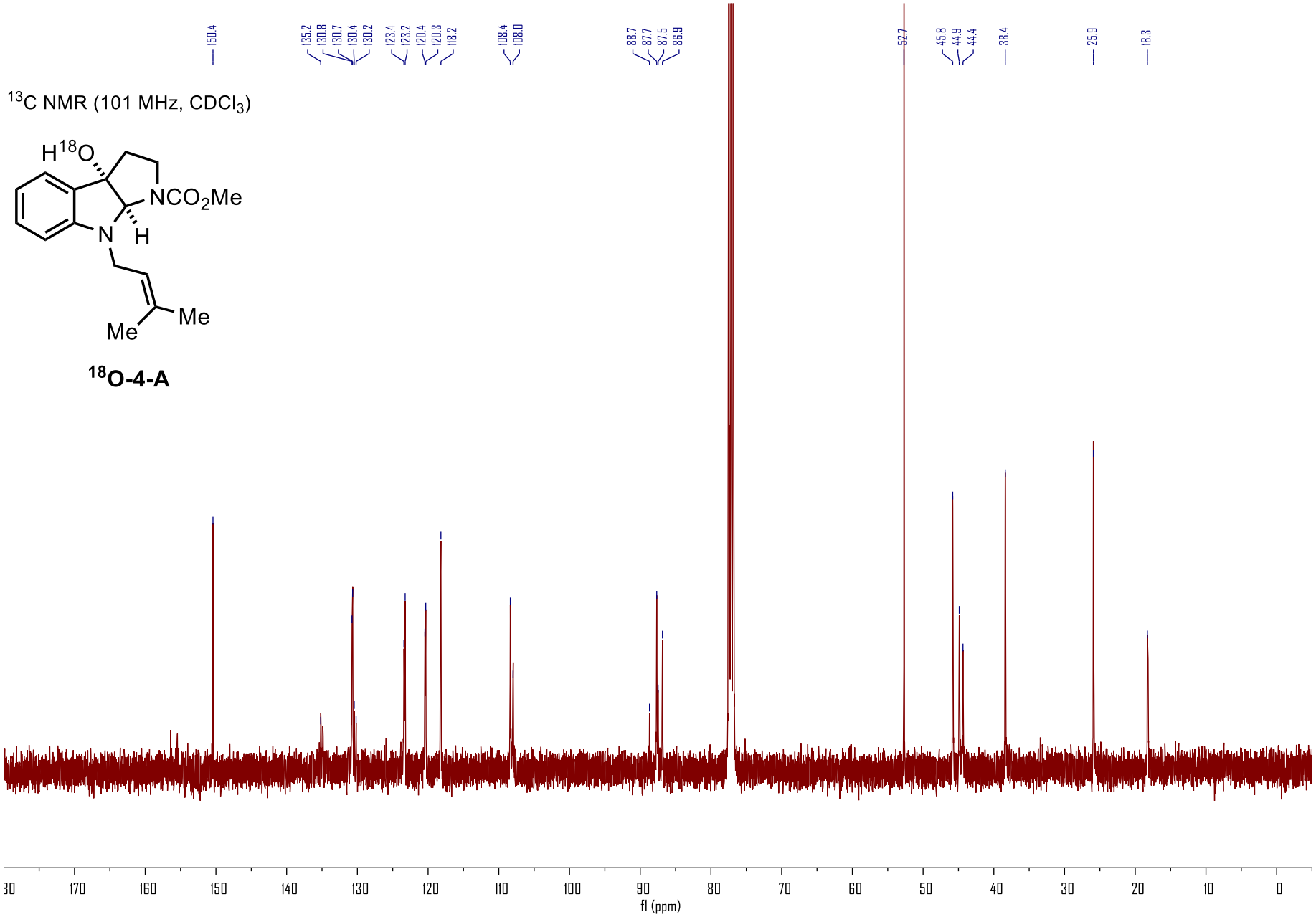

7.99
7.97
7.56
7.54
7.52
7.47
7.45
7.43
7.41
7.39
7.22
7.20
7.18
6.73
6.71
6.69
6.55
6.53
6.51
5.88
5.83
5.24
4.31
4.29
4.27
4.25
4.10
4.07
4.04
3.95
3.93
3.91
3.78
3.75
3.22
3.20
3.19
3.18
3.15
3.13
2.93
2.91
2.89
2.88
2.83
2.82
2.80
2.79
2.71
2.68
2.66
2.63
1.80
1.76
1.71
1H NMR (400 MHz, CDCl3)
O
18O
NCO2Me
N H
Me
Me
18O-3-A
1.99
1.56
0.47
2.08
1.12
1.01
1.00
0.93
0.97
0.54
2.00
0.57
3.26
1.10
1.07
1.08
3.10
3.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


165.2
155.9
155.1
152.1
134.8
134.4
133.2
131.1
130.4
128.8
128.4
127.0
126.8
126.0
125.5
121.3
121.0
118.2
108.4
108.0
94.6
93.7
85.0
84.4
52.7
45.6
45.5
45.3
45.0
37.6
25.9
18.3
18.2
^{13}C NMR (101 MHz, $CDCl_3$)
^{18}O
NCO$_2$Me
N
H
Me
Me
^{18}O-3-A
f1 (ppm)

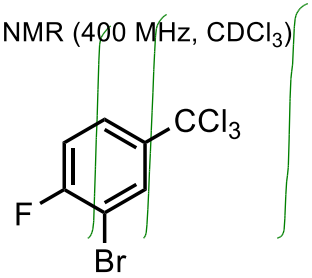
^{1}H NMR (400 MHz, $CDCl_3$)



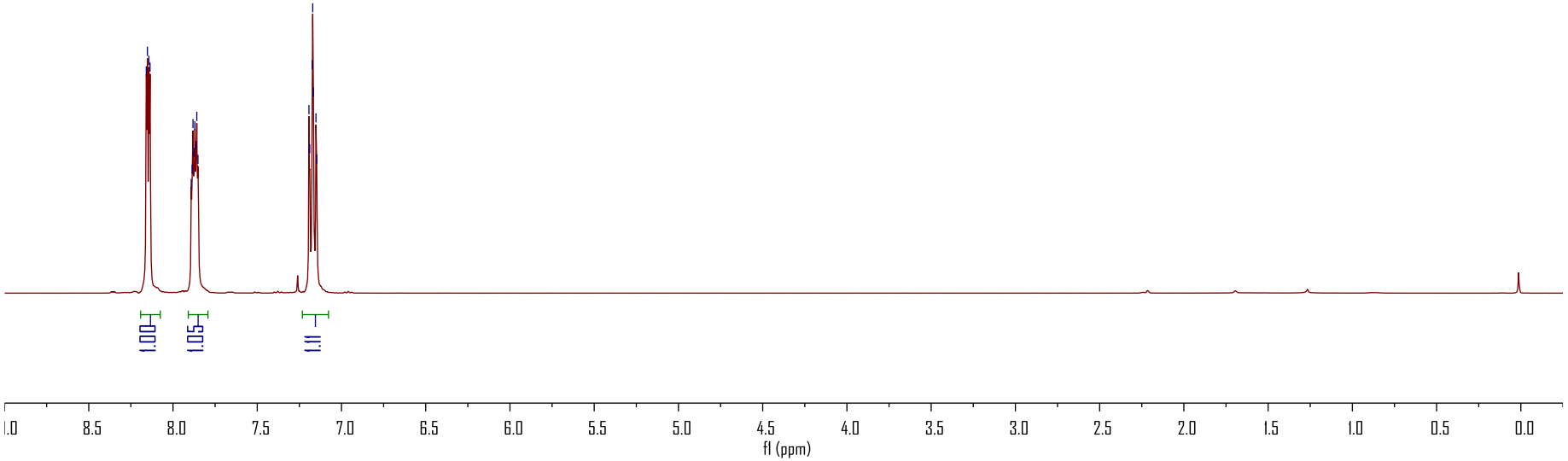
^{18}O-4-A

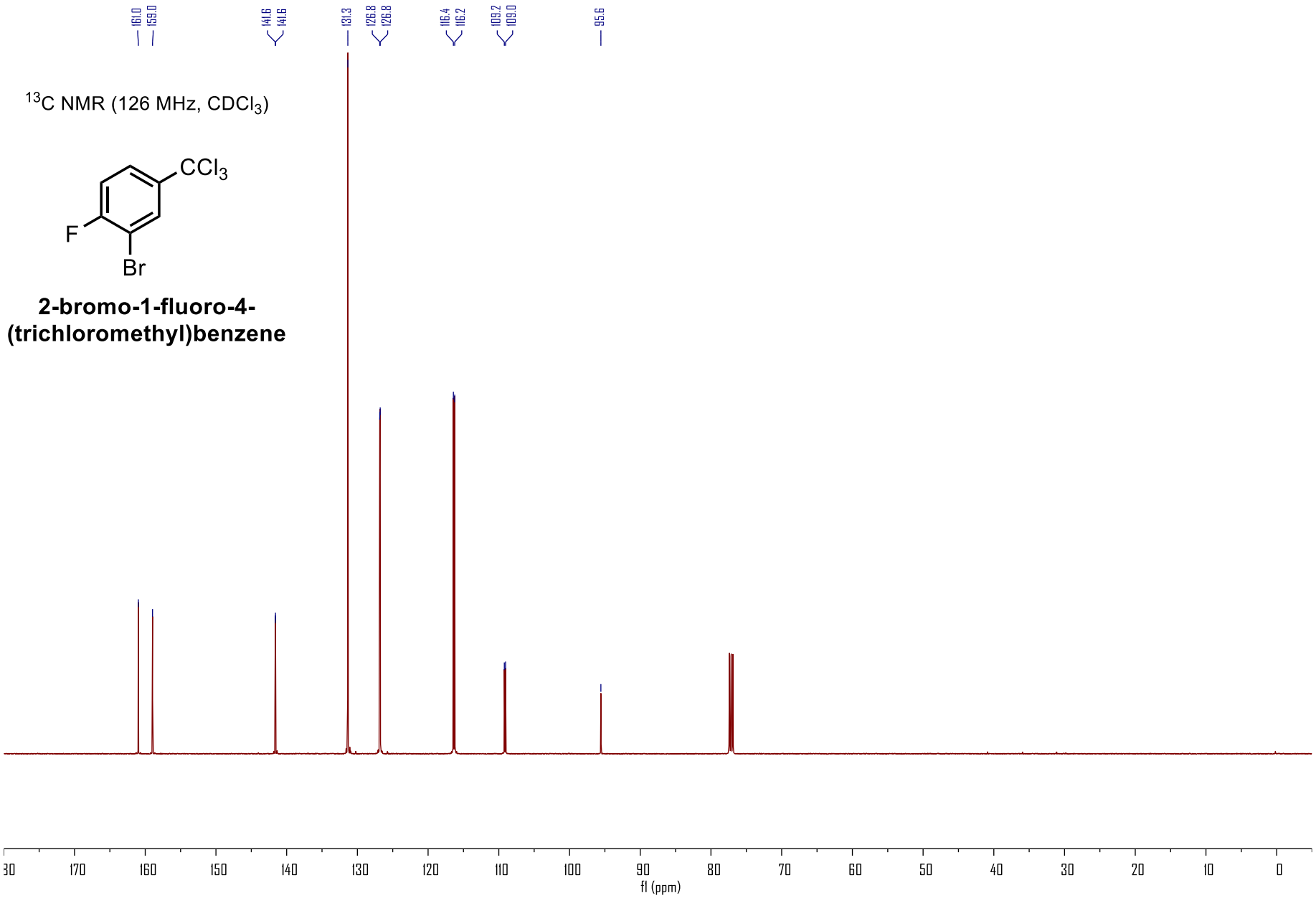

150.4
135.2
130.8
130.7
130.4
130.2
123.4
123.2
120.4
120.3
118.2
108.4
108.0
88.7
87.7
87.5
86.9
52.7
45.8
44.9
44.4
38.4
25.9
18.3
^{13}C NMR (101 MHz, $CDCl_3$)
H^{18}O
NCO$_2$Me
N
H
Me
Me
^{18}O-4-A
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR (400 MHz, $CDCl_3$)

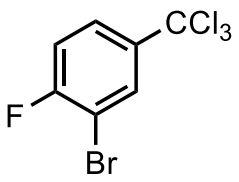


2-bromo-1-fluoro-4-(trichloromethyl)benzene

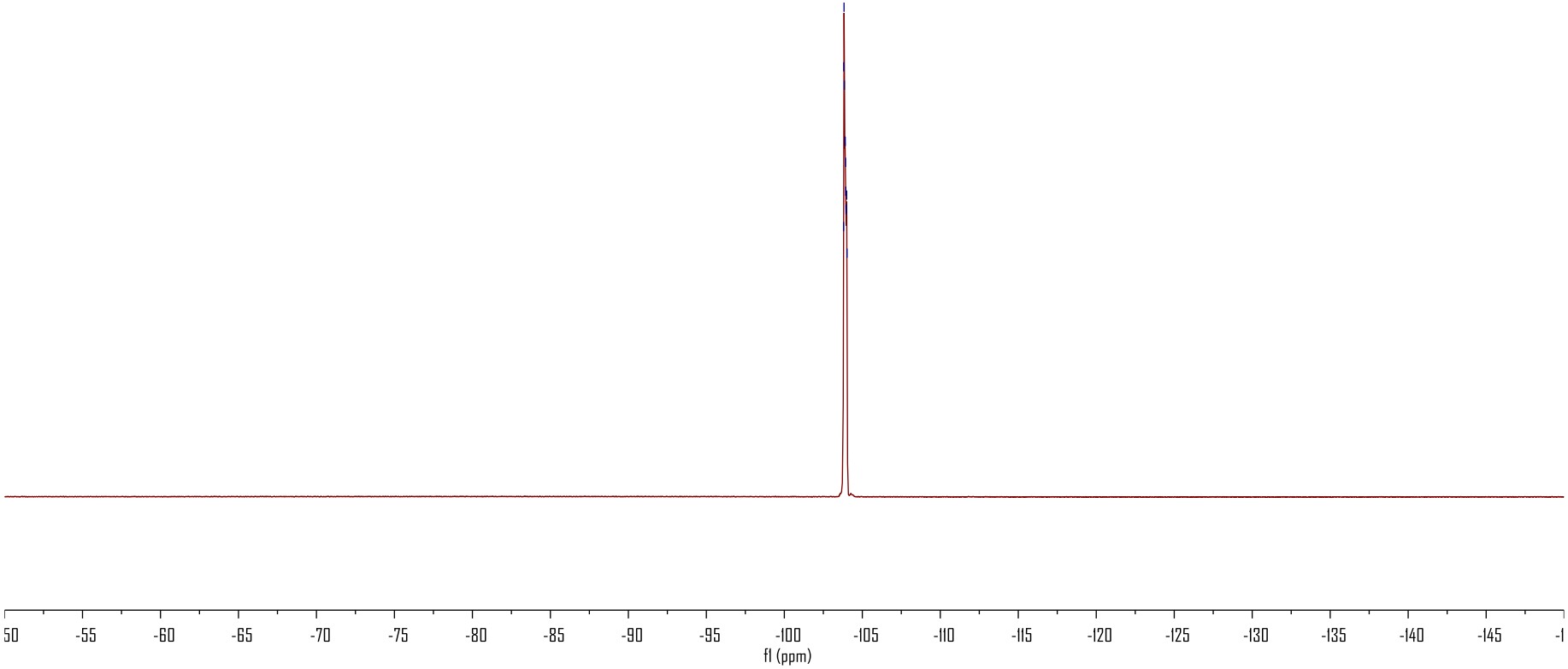


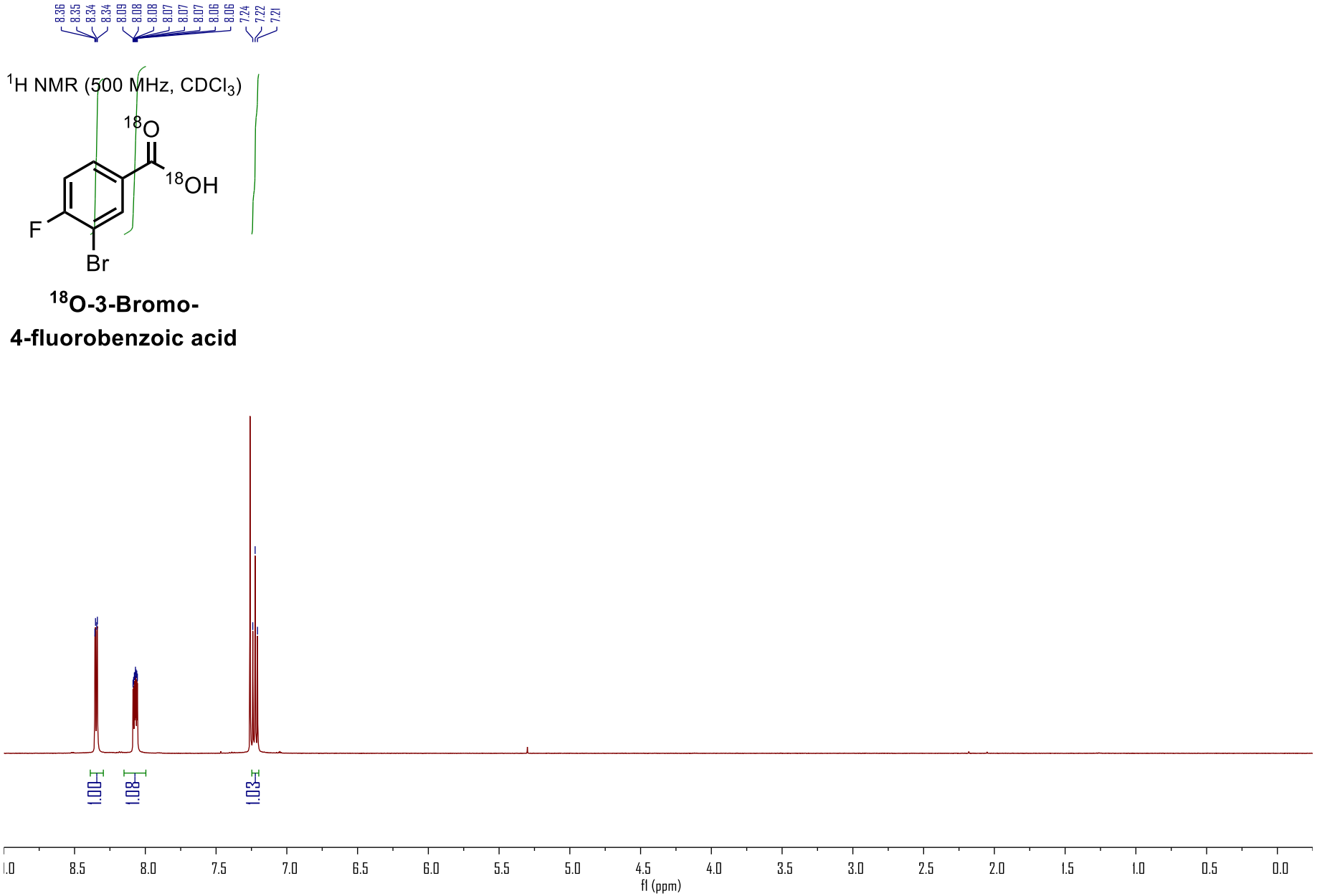

161.0
159.0
141.6
141.6
131.3
126.8
126.8
116.4
116.2
109.2
109.0
95.6
^{13}C NMR (126 MHz, $CDCl_3$)
CCl_3
F
Br
2-bromo-1-fluoro-4-(trichloromethyl)benzene
f1 (ppm)

^{19}F NMR (376 MHz, $CDCl_3$)

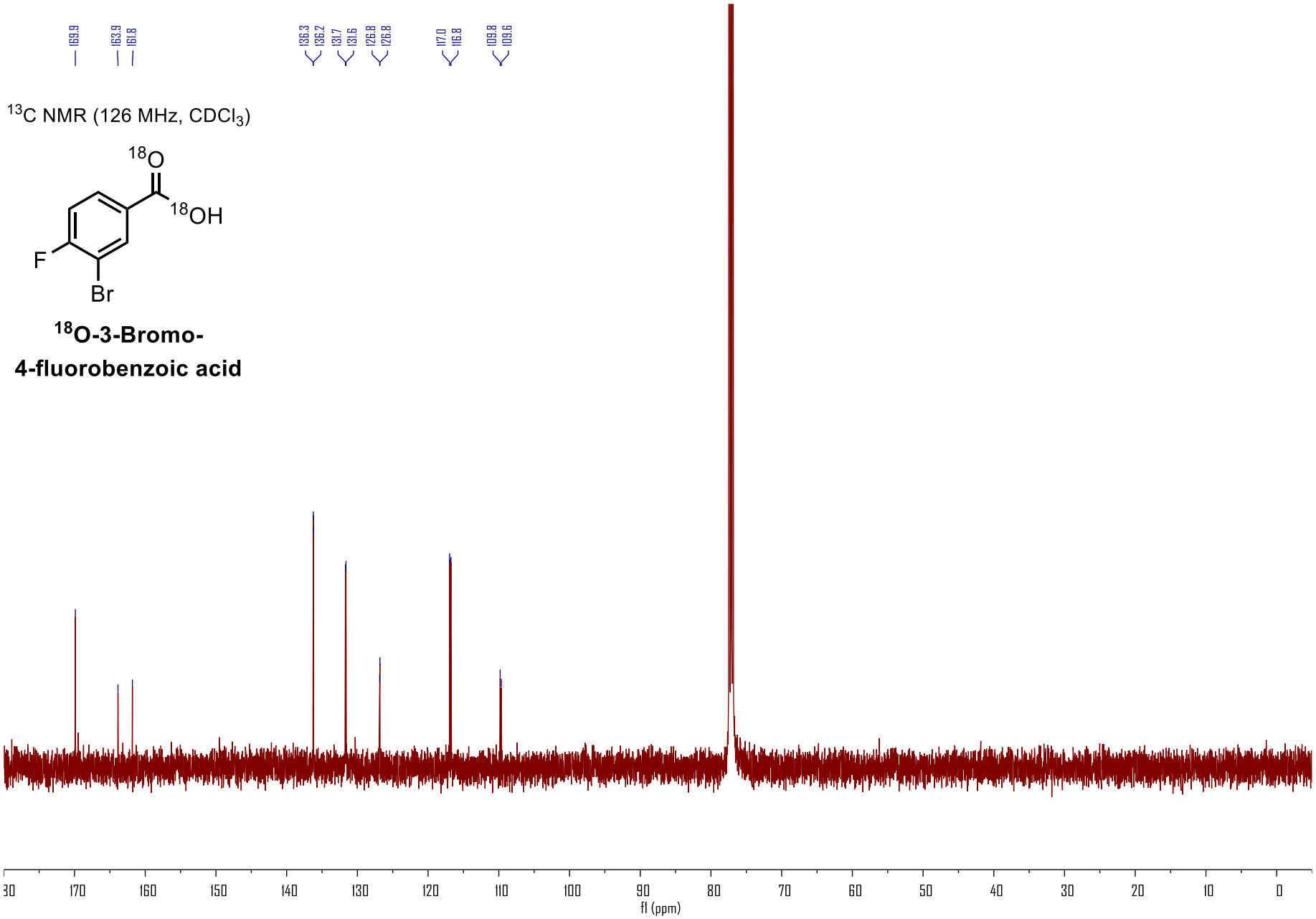


2-bromo-1-fluoro-4-(trichloromethyl)benzene

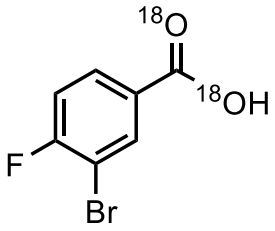




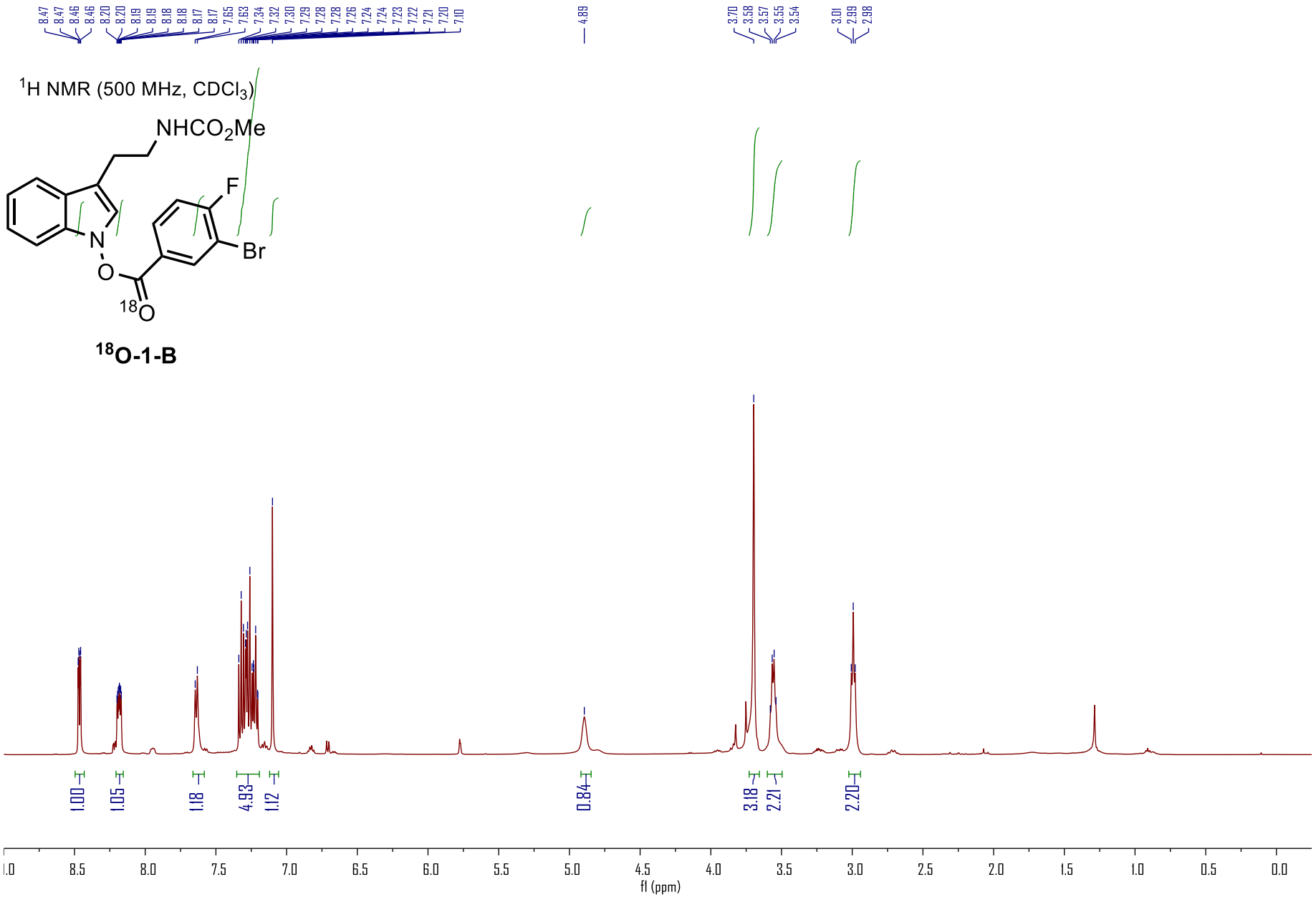
^{18}O-3-Bromo-4-fluorobenzoic acid

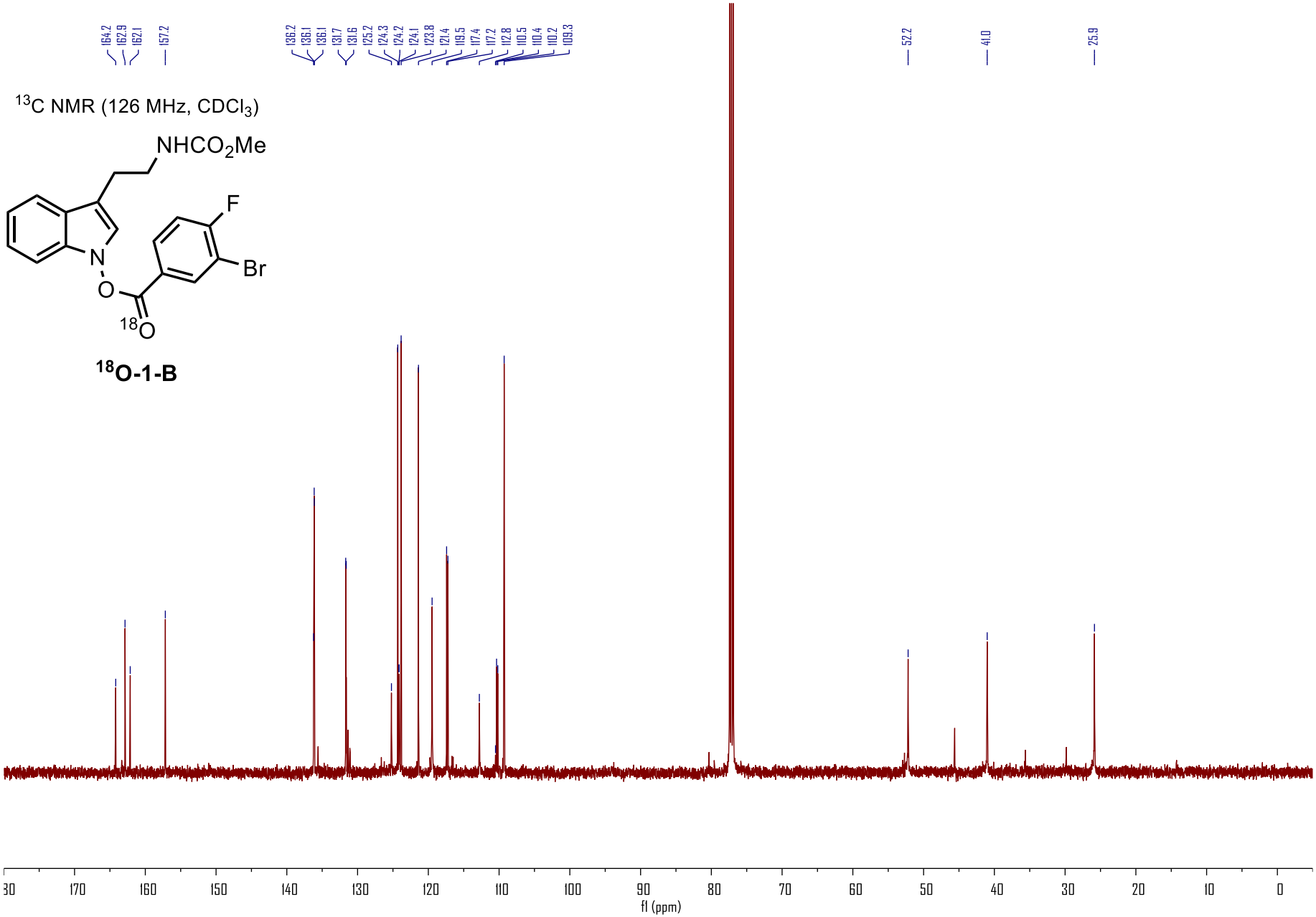

169.9
163.9
161.8
136.3
136.2
131.7
131.6
126.8
126.8
117.0
116.8
109.8
109.6
^{13}C NMR (126 MHz, $CDCl_3$)
^{18}O
^{18}OH
F
Br
^{18}O-3-Bromo-
4-fluorobenzoic acid
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

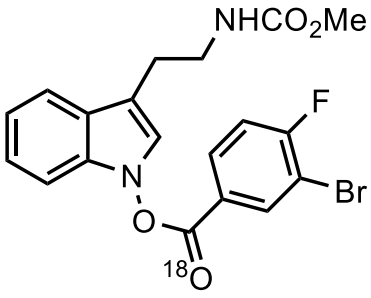


^{18}O-3-Bromo-4-fluorobenzoic acid

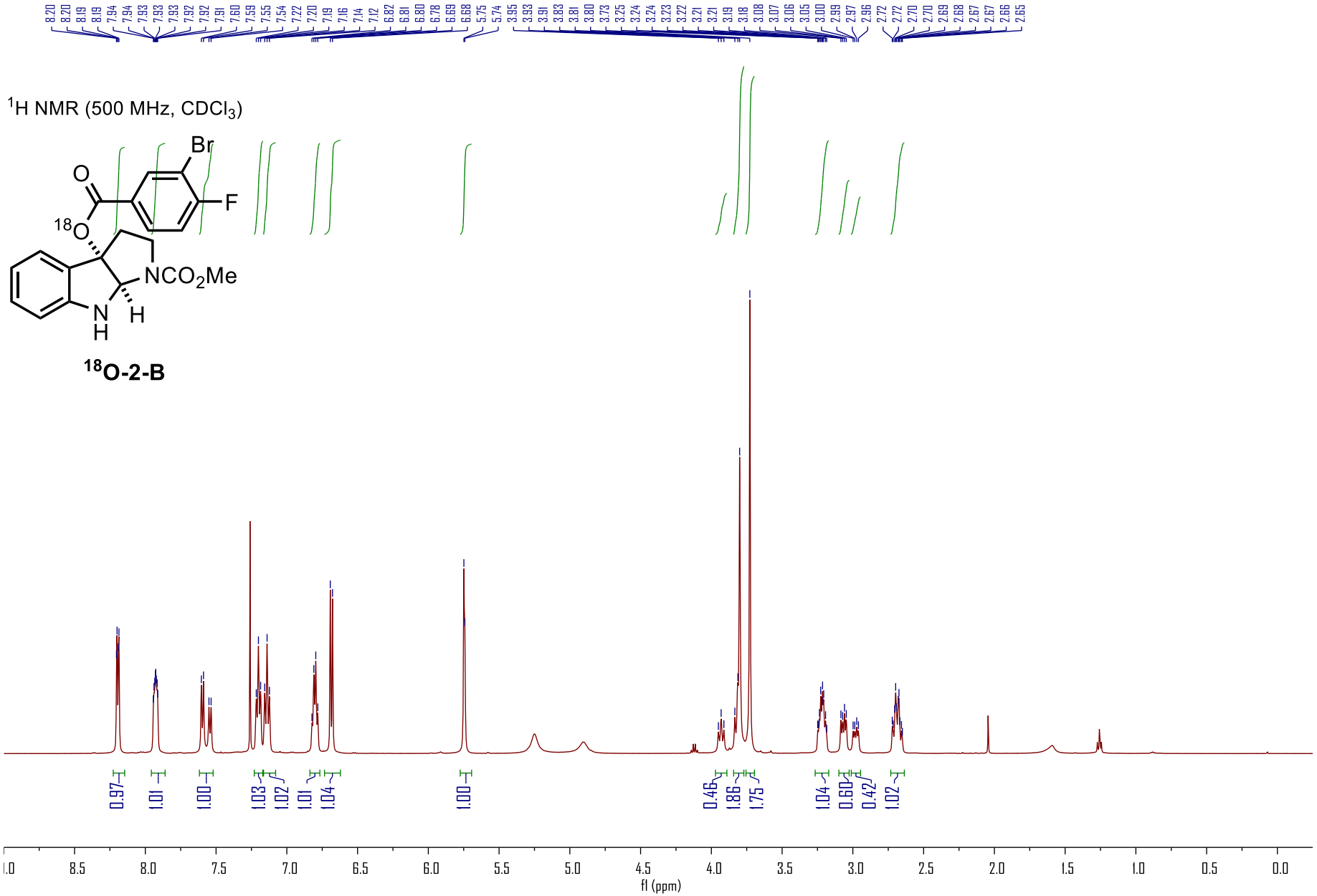

8.47
8.47
8.46
8.46
8.20
8.20
8.19
8.19
8.18
8.18
8.17
8.17
7.65
7.63
7.34
7.32
7.30
7.29
7.28
7.28
7.26
7.24
7.24
7.23
7.22
7.21
7.20
7.10
4.89
3.70
3.58
3.57
3.55
3.54
3.01
2.99
2.98
1H NMR (500 MHz, CDCl3)
NHCO2Me
F
Br
N
O
18O
18O-1-B
1.00
1.05
1.18
4.93
1.12
0.84
3.18
2.21
2.20
f1 (ppm)

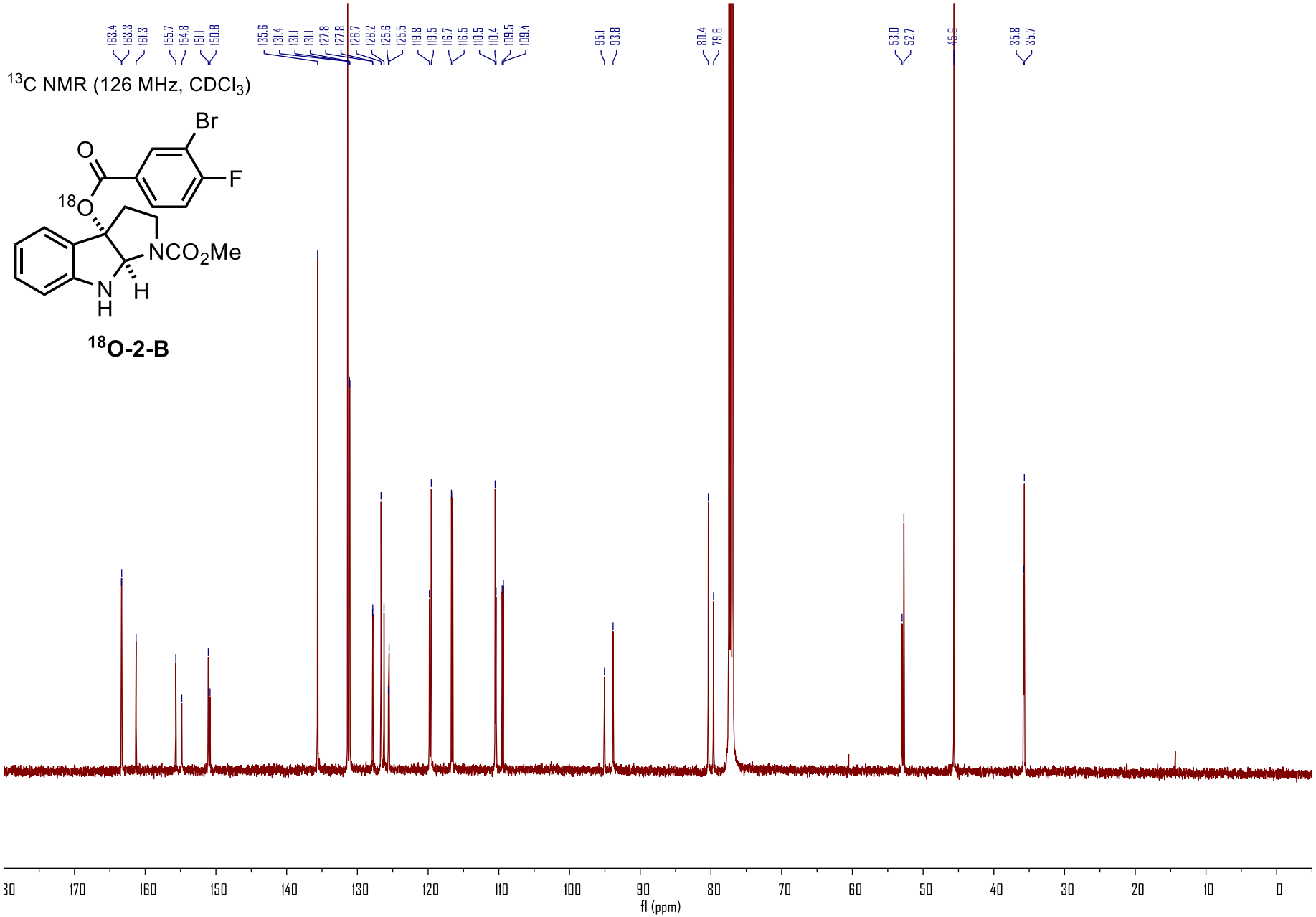

164.2
162.9
162.1
157.2
136.2
136.1
136.1
131.7
131.6
125.2
124.3
124.2
124.1
123.8
121.4
119.5
117.4
117.2
112.8
110.5
110.4
110.2
109.3
52.2
41.0
25.9
13C NMR (126 MHz, CDCl3)
NHCO2Me
F
Br
N
O
18O
18O-1-B
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

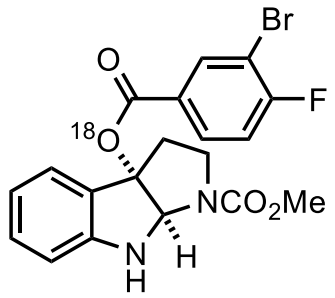


^{18}O-1-B

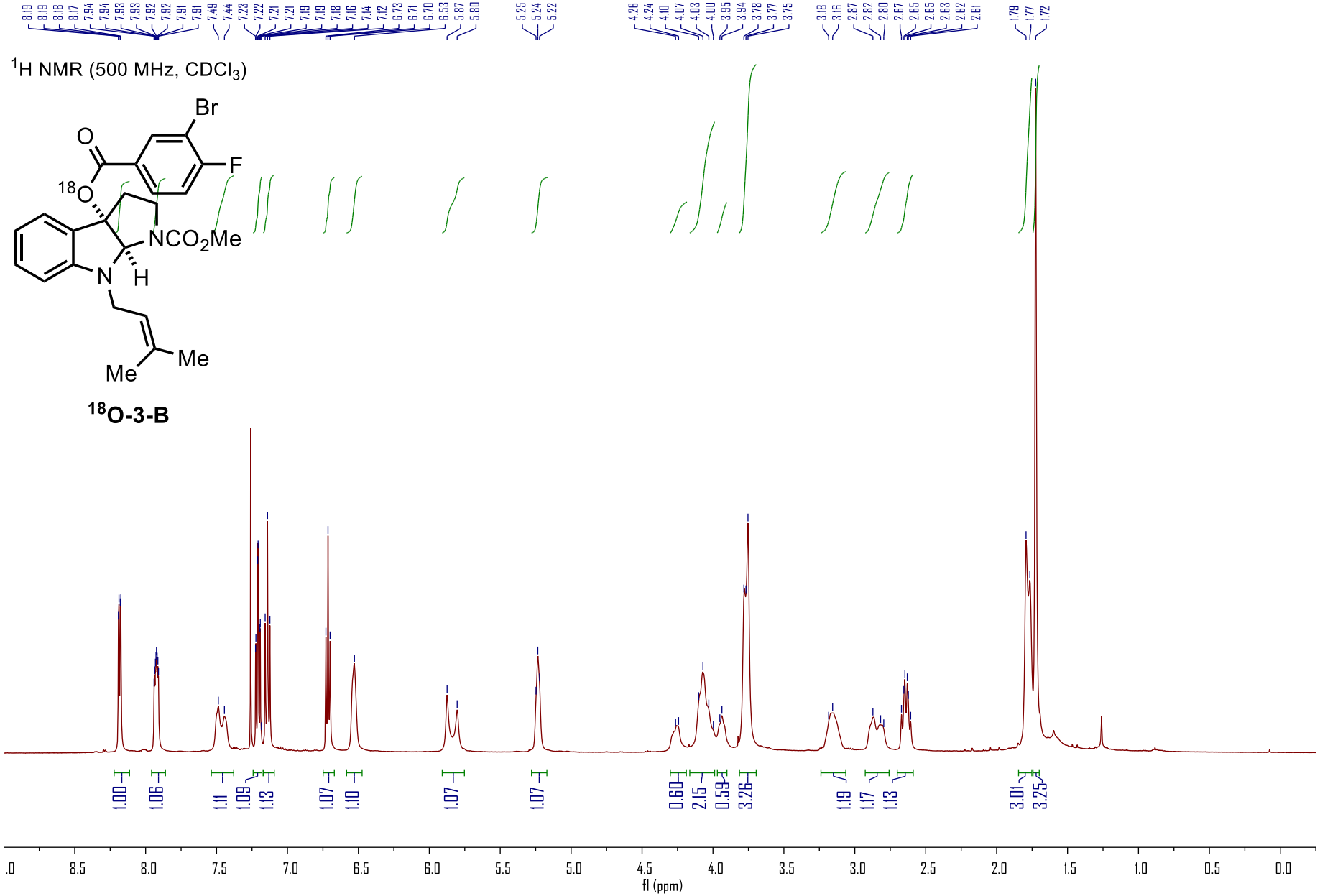

8.20 8.20 8.19 8.19 7.94 7.94 7.93 7.93 7.93 7.92 7.92 7.91 7.60 7.59 7.55 7.54 7.22 7.20 7.19 7.16 7.14 7.12 6.82 6.81 6.80 6.78 6.69 6.68 5.75 5.74 3.95 3.93 3.91 3.83 3.81 3.80 3.73 3.25 3.24 3.24 3.23 3.22 3.21 3.21 3.19 3.18 3.08 3.07 3.06 3.05 3.00 2.99 2.97 2.96 2.72 2.72 2.70 2.70 2.69 2.68 2.67 2.67 2.66 2.65
1H NMR (500 MHz, CDCl3)
Br
O
F
18O
NCO2Me
N
H
H
18O-2-B
0.97 1.01 1.00 1.03 1.02 1.01 1.04 1.00 0.46 1.86 1.75 1.04 0.60 0.42 1.02
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

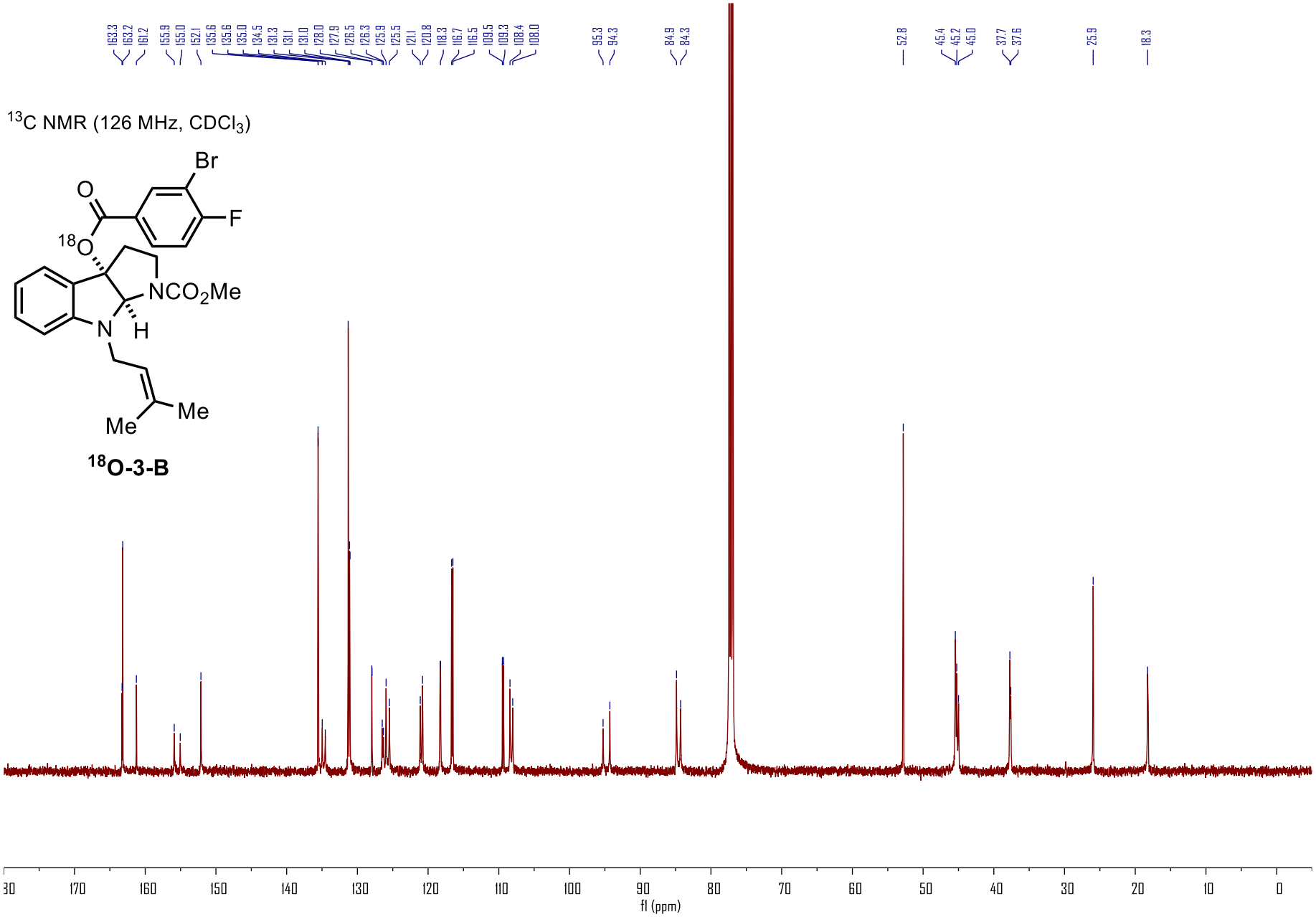

163.4
163.3
161.3
155.7
154.8
151.1
150.8
135.6
131.4
131.1
131.1
127.8
127.8
126.7
126.2
125.6
125.5
119.8
119.5
116.7
116.5
110.5
110.4
109.5
109.4
95.1
93.8
80.4
79.6
53.0
52.7
45.6
35.8
35.7
^{13}C NMR (126 MHz, $CDCl_3$)
Br
O
F
^{18}O
NCO_2Me
N
H
H
^{18}O-2-B
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

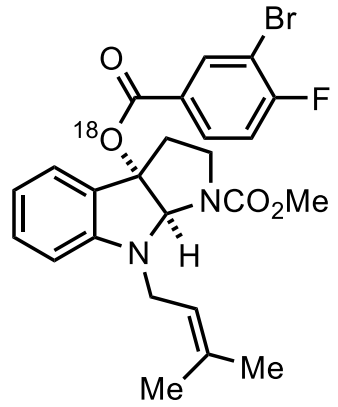


^{18}O-2-B

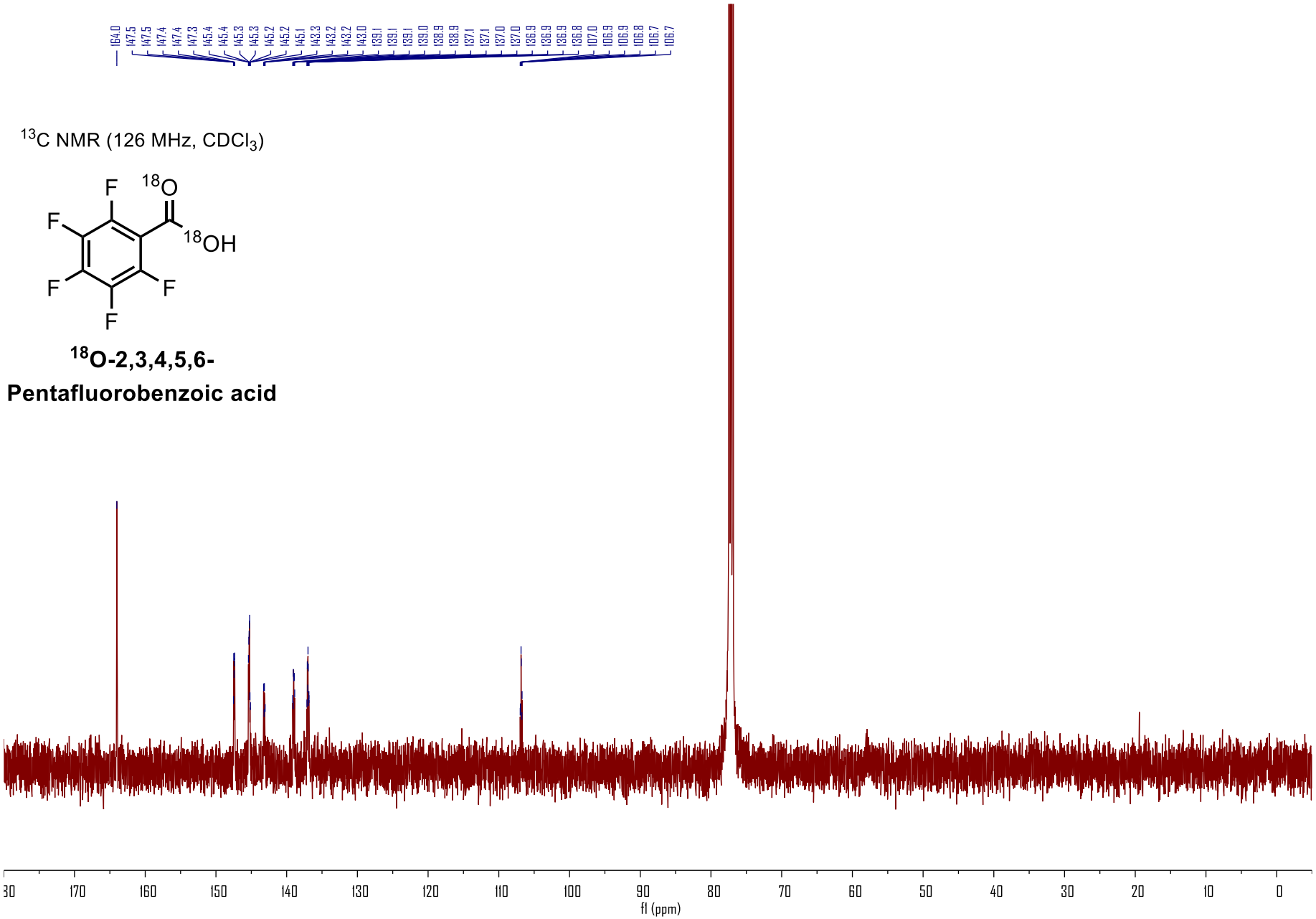

^{1}H NMR (500 MHz, $CDCl_3$)
Br
O
F
^{18}O
NCO_2Me
N
H
Me
Me
^{18}O-3-B
f1 (ppm)


163.3
163.2
161.2
155.9
155.0
152.1
135.6
135.6
135.0
134.5
131.3
131.1
131.0
128.0
127.9
126.5
126.3
125.9
125.5
121.1
120.8
118.3
116.7
116.5
109.5
109.3
108.4
108.0
95.3
94.3
84.9
84.3
52.8
45.4
45.2
45.0
37.7
37.6
25.9
18.3
13C NMR (126 MHz, CDCl3)
Br
O
F
18O
NCO2Me
N
H
Me
Me
18O-3-B
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

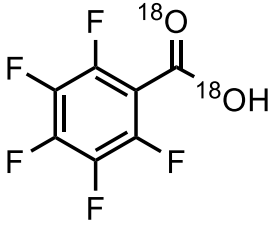
^{19}F NMR (471 MHz, $CDCl_3$)



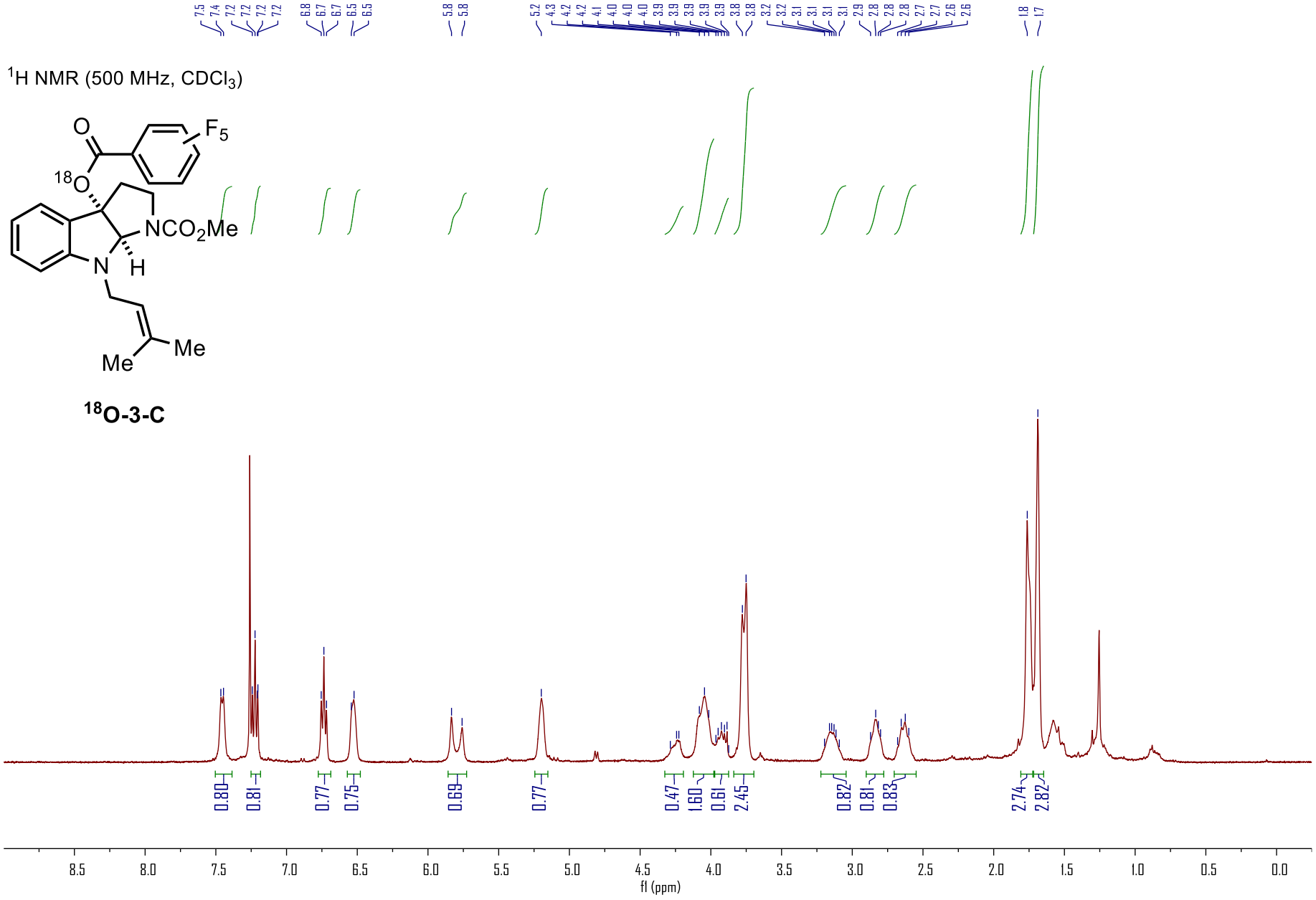
^{18}O-3-B

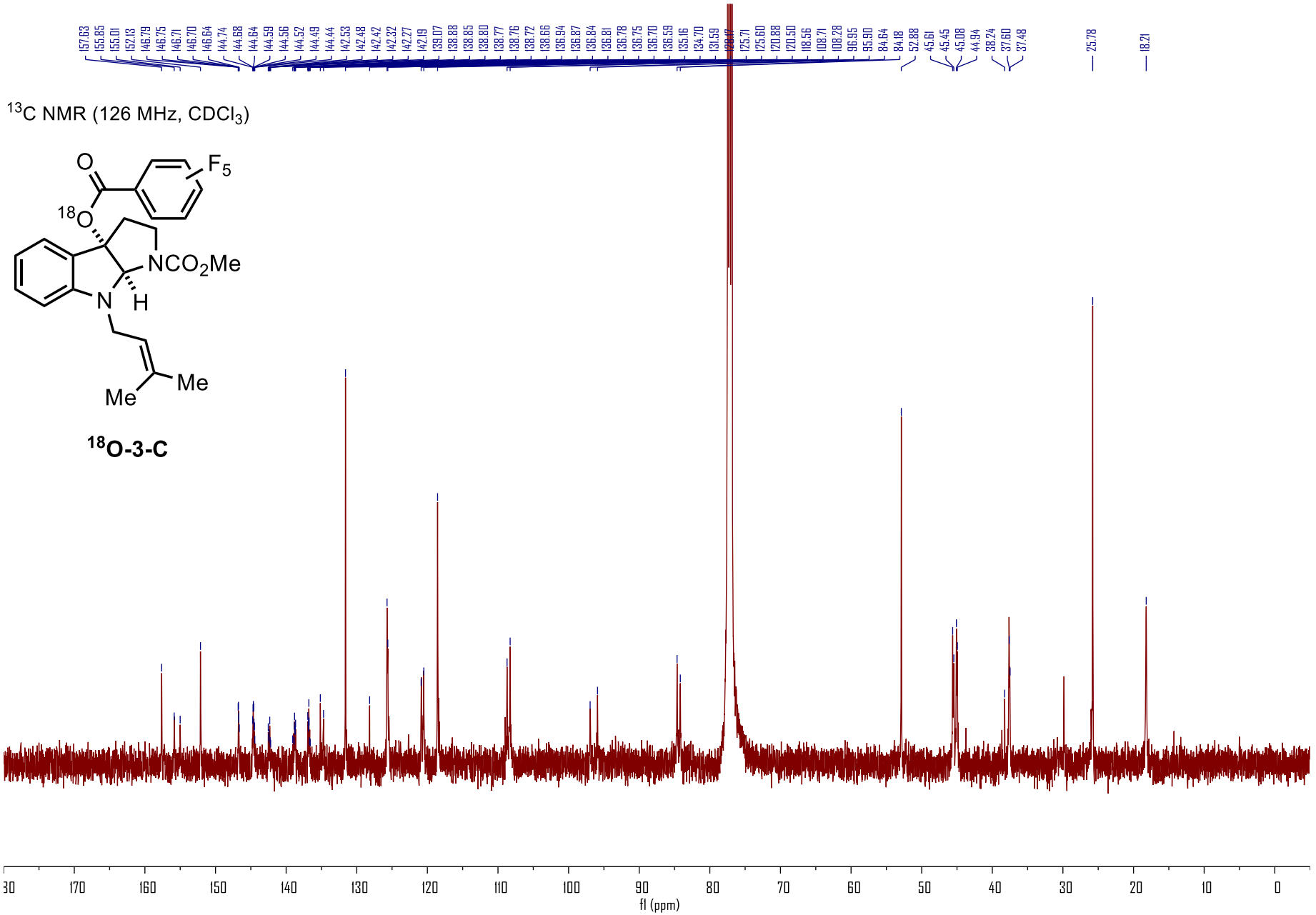

164.0
147.5
147.5
147.4
147.4
147.3
145.4
145.4
145.3
145.3
145.2
145.2
145.1
143.3
143.2
143.2
143.0
139.1
139.1
139.1
139.0
138.9
138.9
137.1
137.1
137.0
137.0
136.9
136.9
136.9
136.8
107.0
106.9
106.9
106.8
106.7
106.7
^{13}C NMR (126 MHz, $CDCl_3$)
F
^{18}O
F
^{18}OH
F
F
F
^{18}O-2,3,4,5,6-
Pentafluorobenzoic acid
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

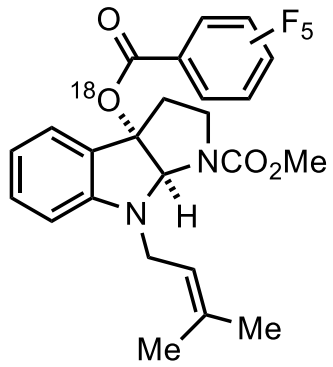


^{18}O-2,3,4,5,6-Pentafluorobenzoic acid

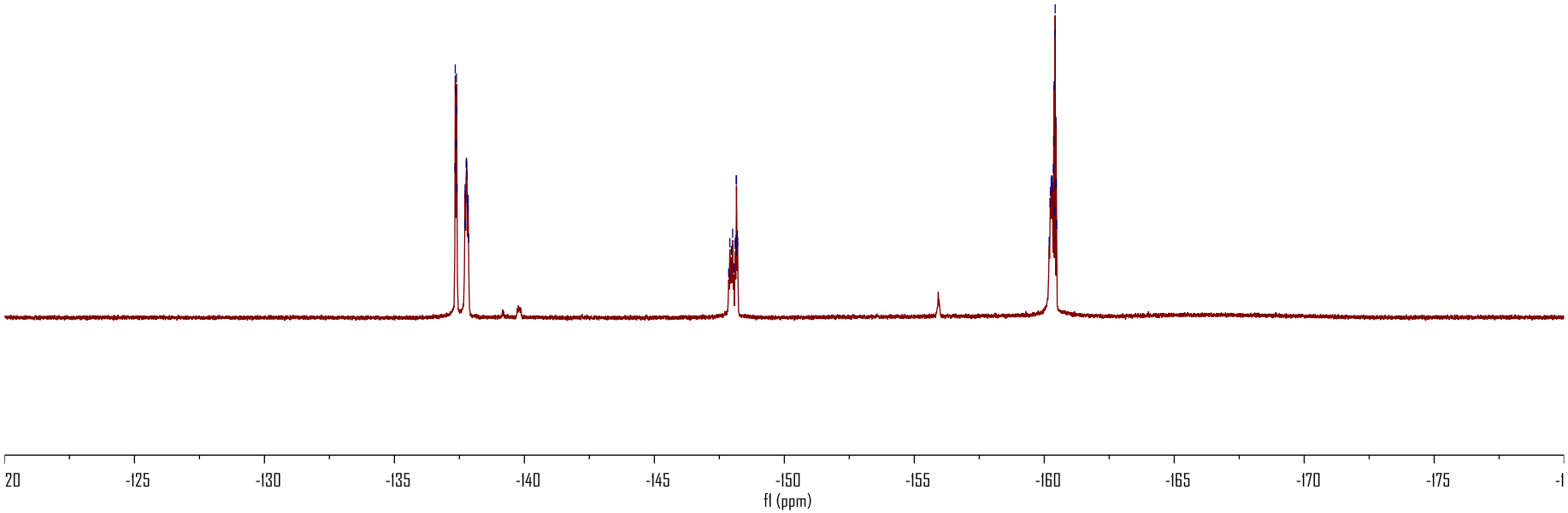

1H NMR (500 MHz, CDCl3)
18O-3-C
F5
NCO2Me
Me
Me
f1 (ppm)

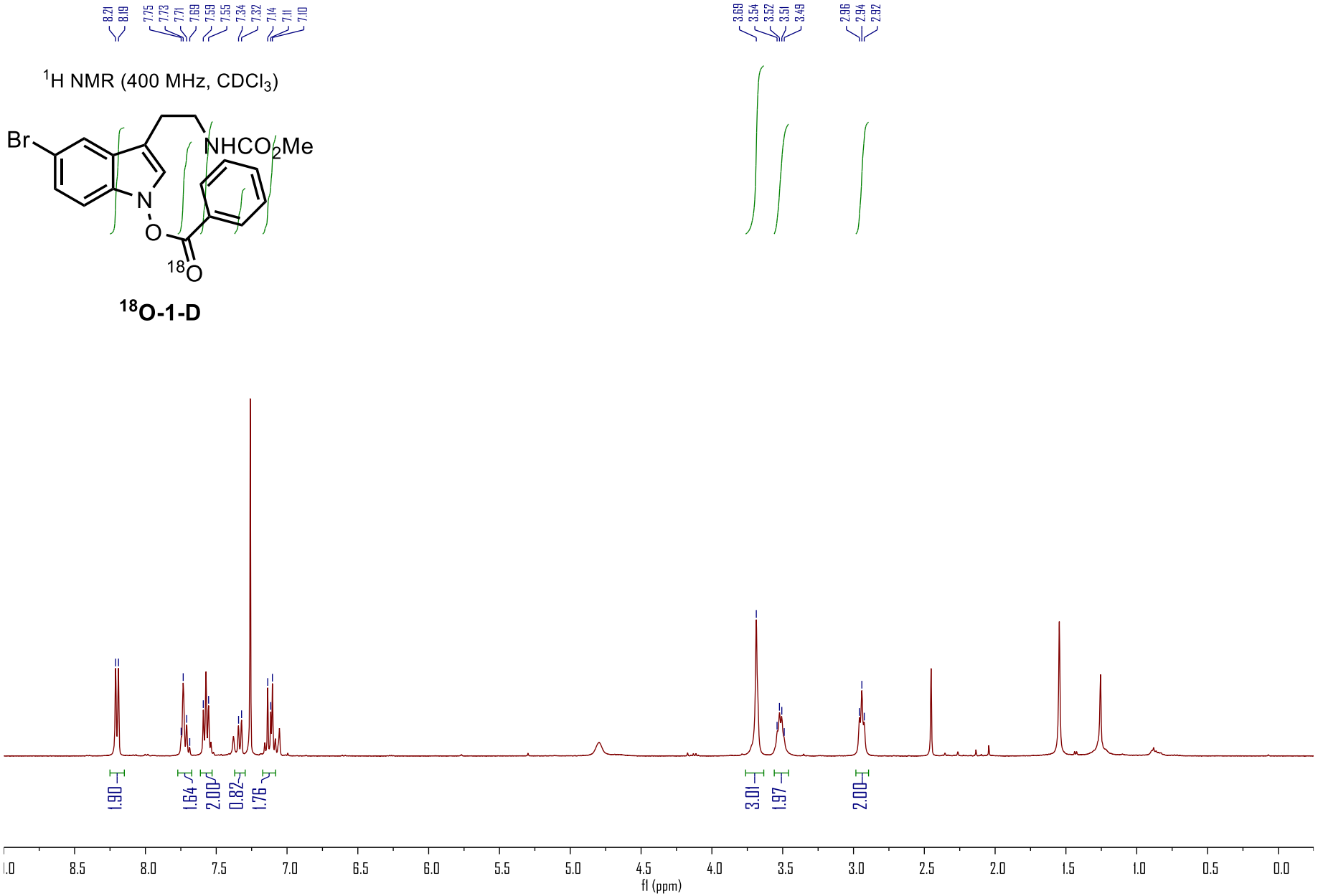

157.63
155.85
155.01
152.13
146.79
146.75
146.71
146.70
146.64
144.74
144.68
144.64
144.59
144.56
144.52
144.49
144.44
142.53
142.48
142.42
142.32
142.27
142.19
139.07
138.88
138.85
138.80
138.77
138.76
138.72
138.66
136.94
136.87
136.84
136.81
136.78
136.75
136.70
136.59
135.16
134.70
131.59
125.71
125.60
120.88
120.50
118.56
108.71
108.28
96.95
95.90
84.64
84.18
52.88
45.61
45.45
45.08
44.94
38.24
37.60
37.48
25.78
18.21
^{13}C NMR (126 MHz, CDCl$_3$)
O
F$_5$
^{18}O
NCO$_2$Me
N
H
Me
Me
^{18}O-3-C
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

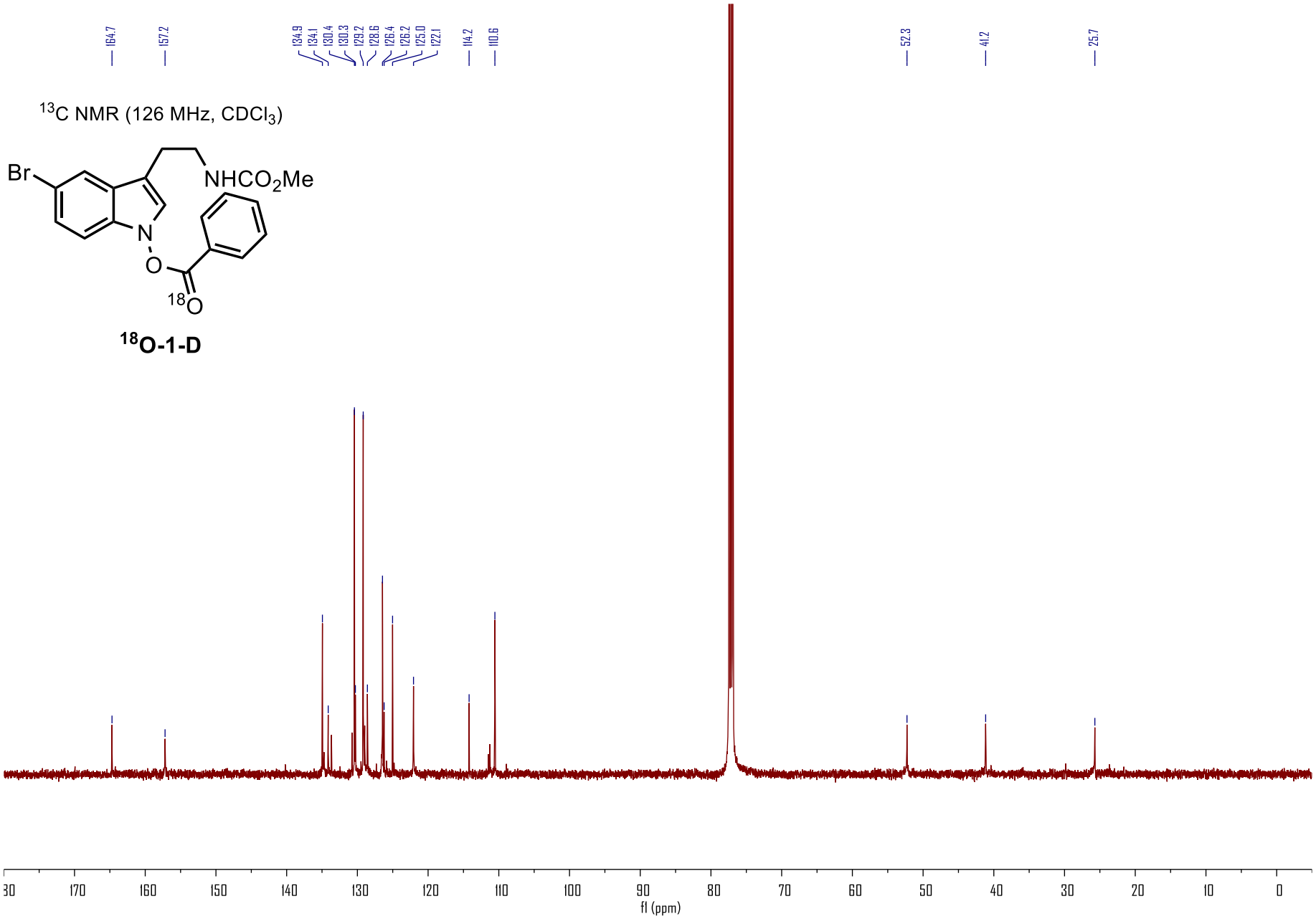
^{19}F NMR (471 MHz, $CDCl_3$)

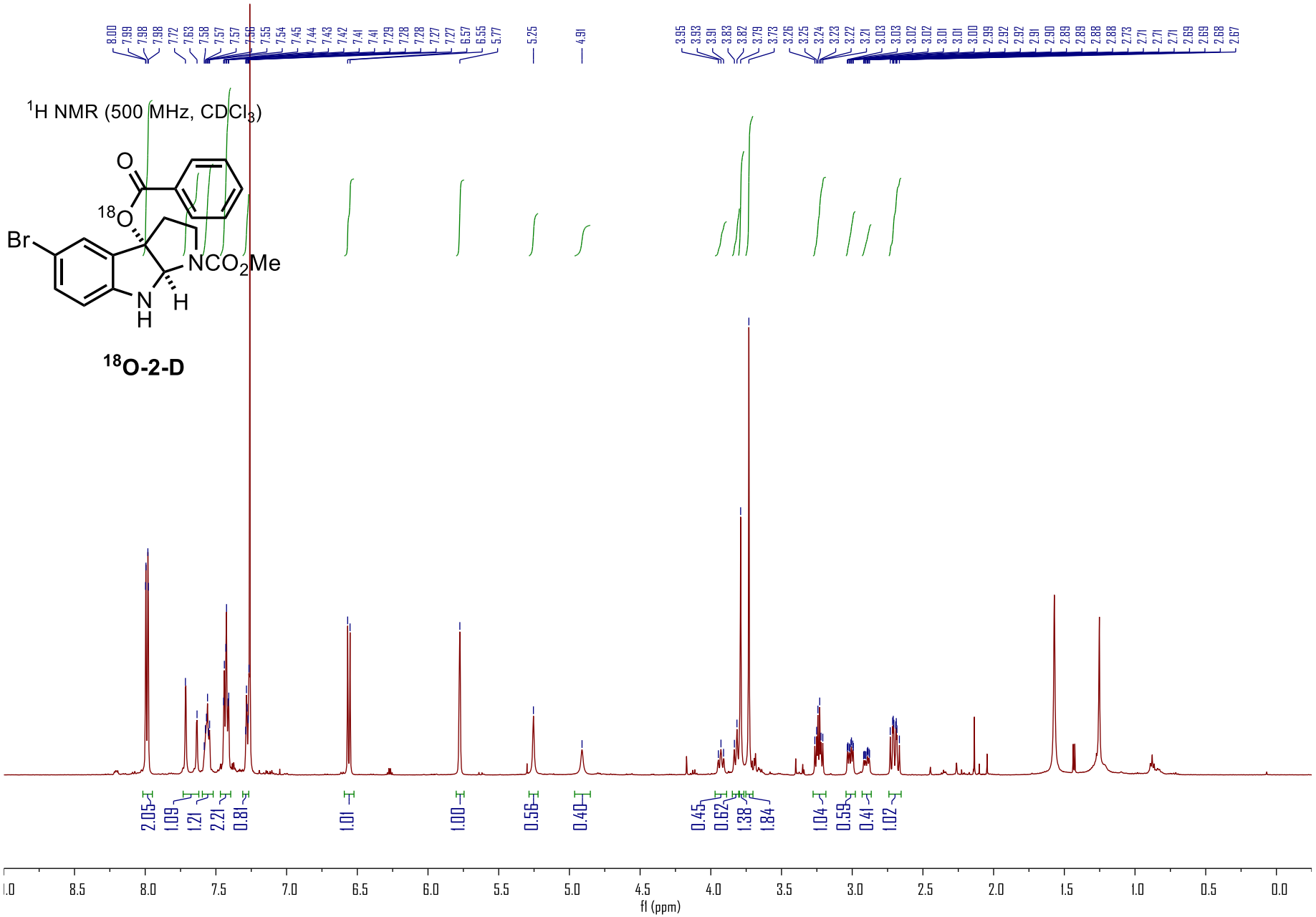


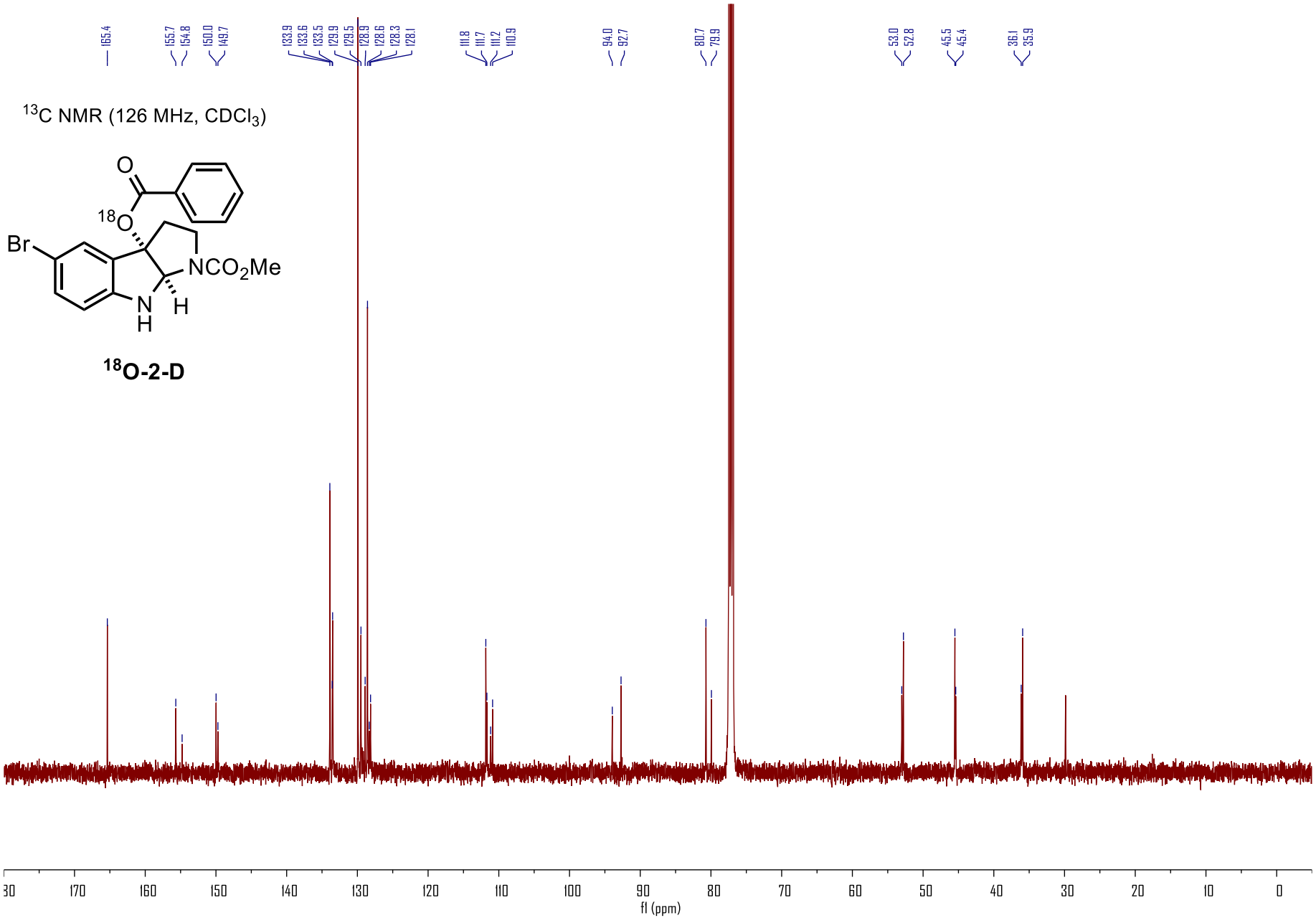
^{18}O-3-C

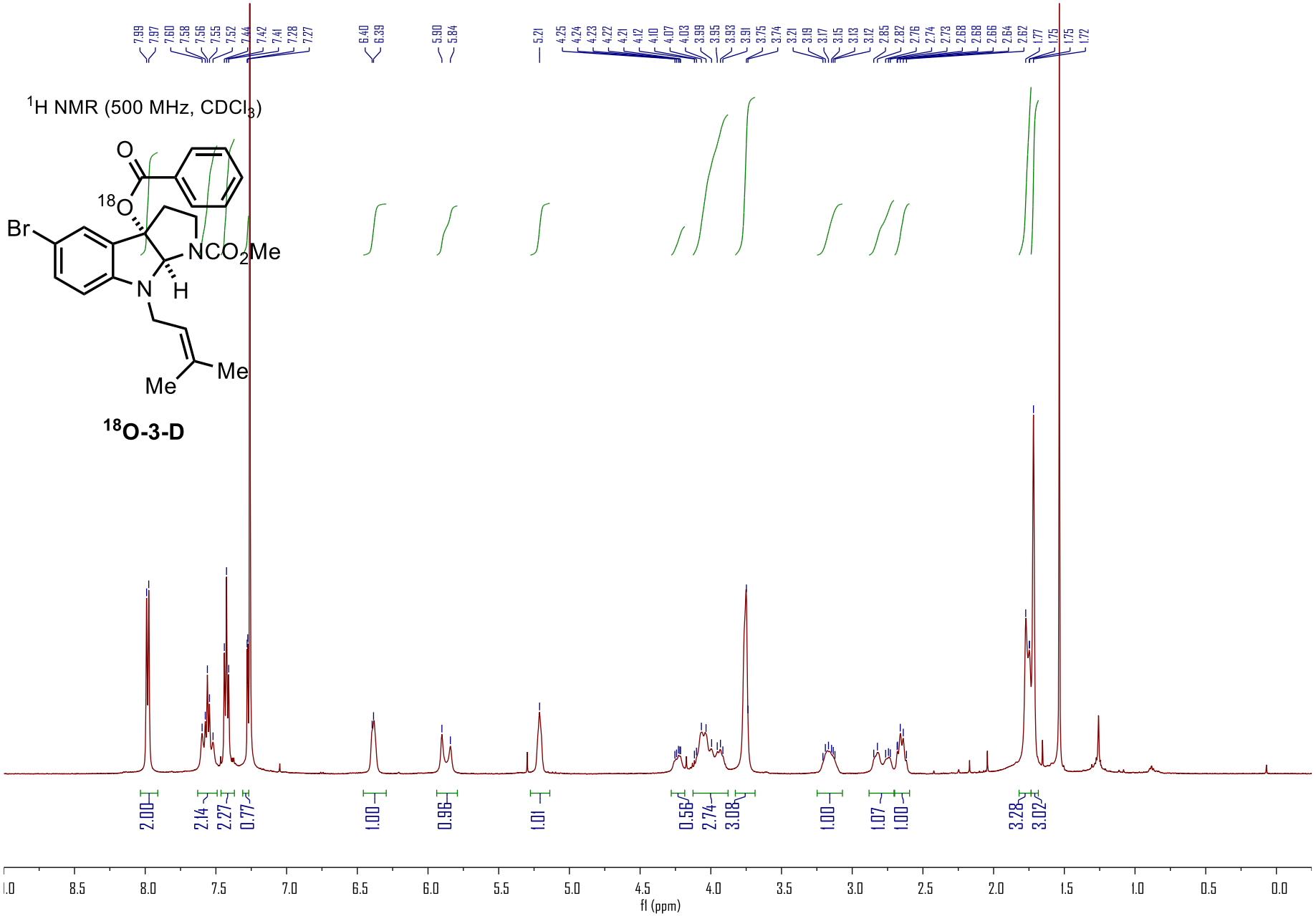


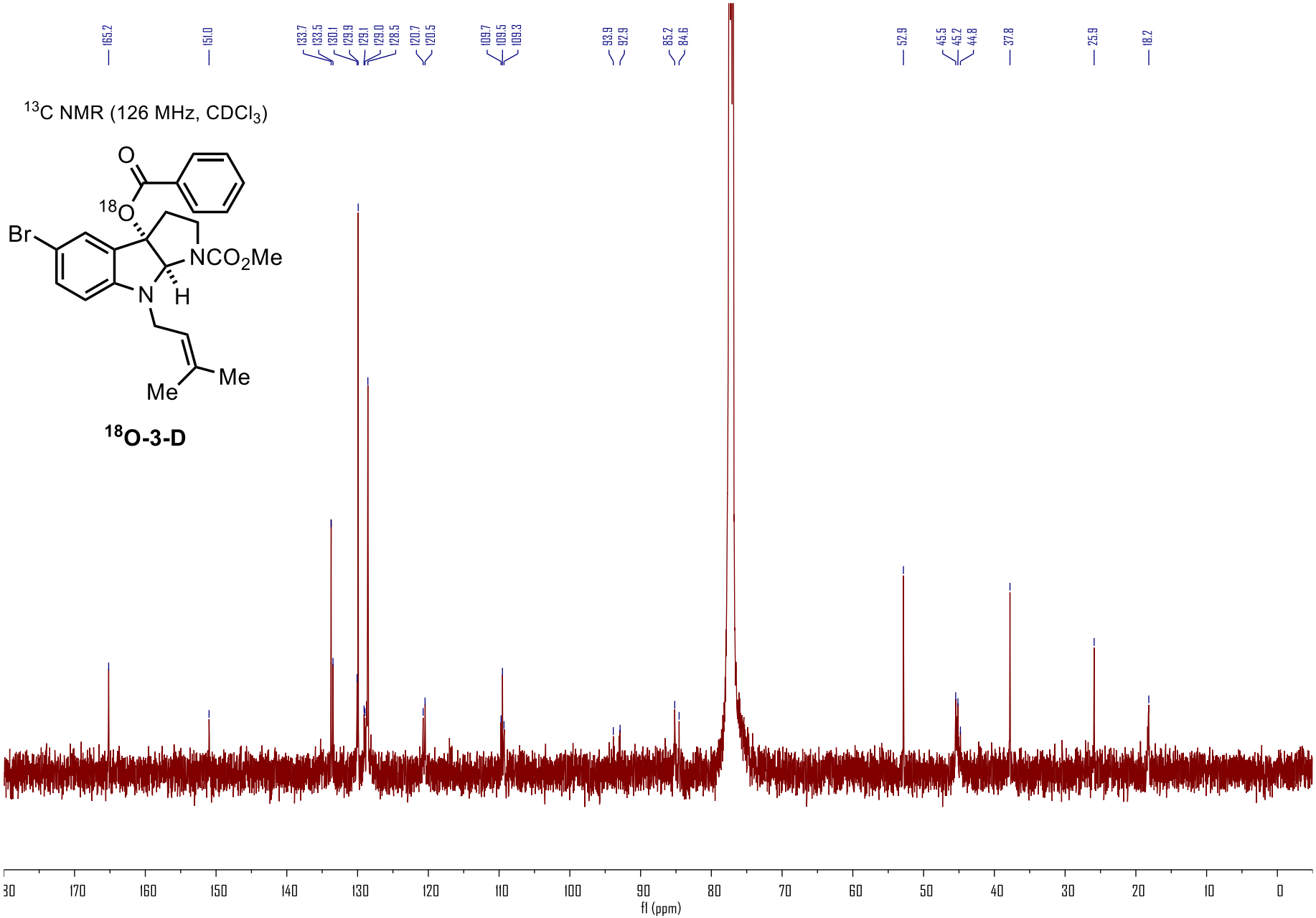

8.21
8.19
7.75
7.73
7.71
7.69
7.59
7.55
7.34
7.32
7.14
7.11
7.10
3.69
3.54
3.52
3.51
3.49
2.96
2.94
2.92
^{1}H NMR (400 MHz, $CDCl_3$)
Br
$NHCO_2Me$
N
O
^{18}O
^{18}O-1-D
1.90
1.64
2.00
0.82
1.76
3.01
1.97
2.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

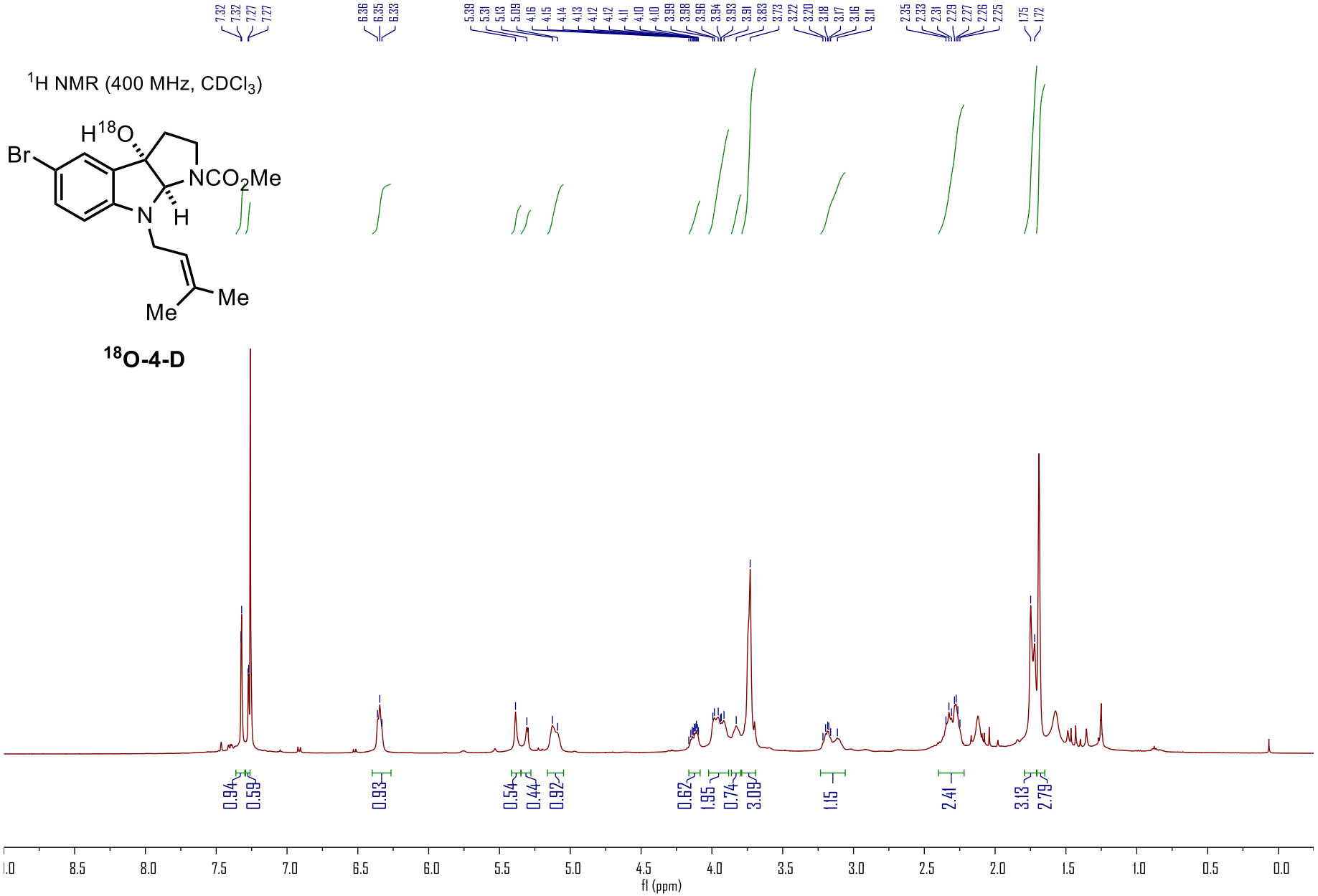

164.7
157.2
134.9
134.1
130.4
130.3
129.2
128.6
126.4
126.2
125.0
122.1
114.2
110.6
52.3
41.2
25.7
13C NMR (126 MHz, CDCl3)
Br
NHCO2Me
N
O
18O
18O-1-D
f1 (ppm)

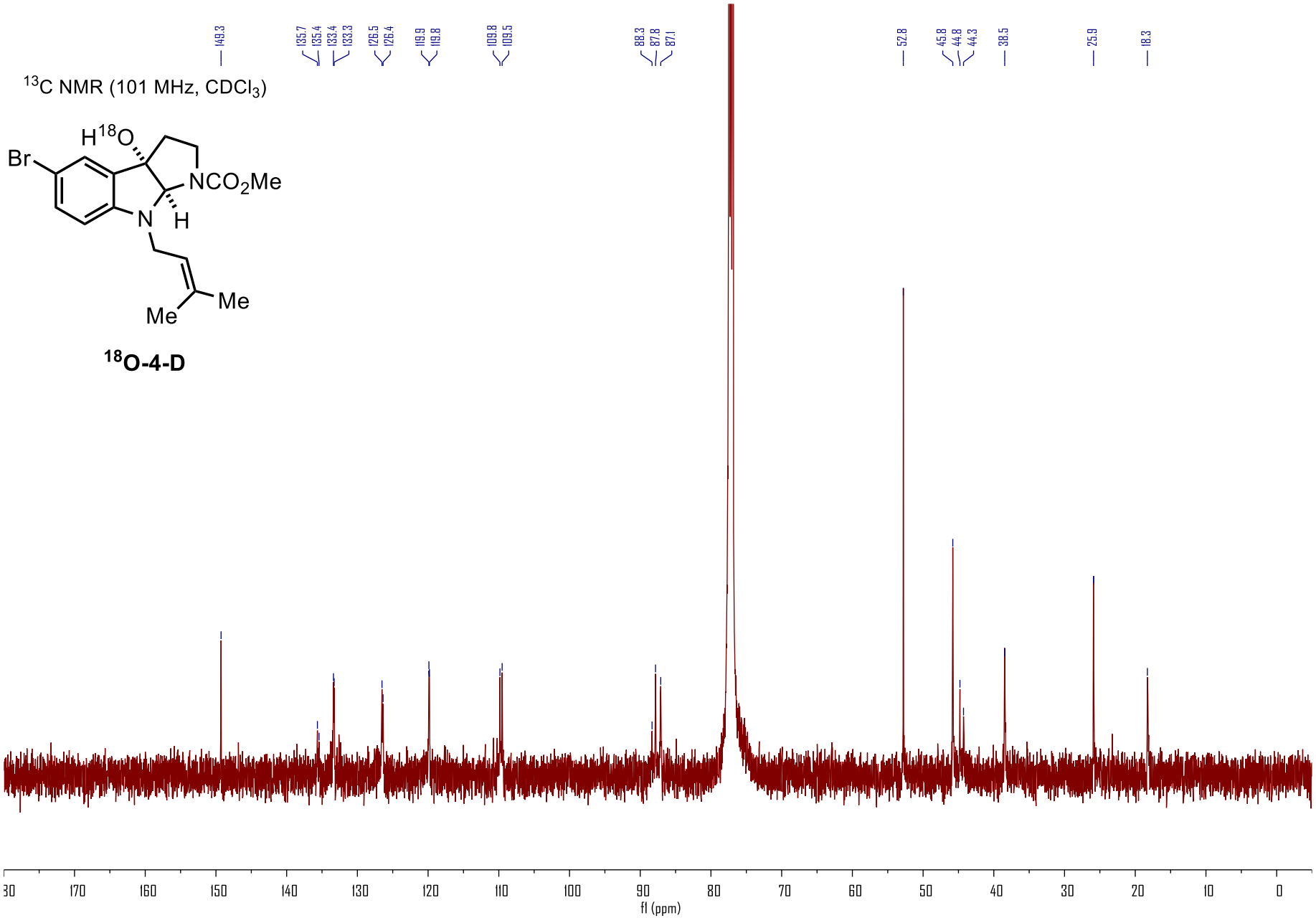

^{1}H NMR (500 MHz, CDCl$_3$)
^{18}O-2-D
fl (ppm)

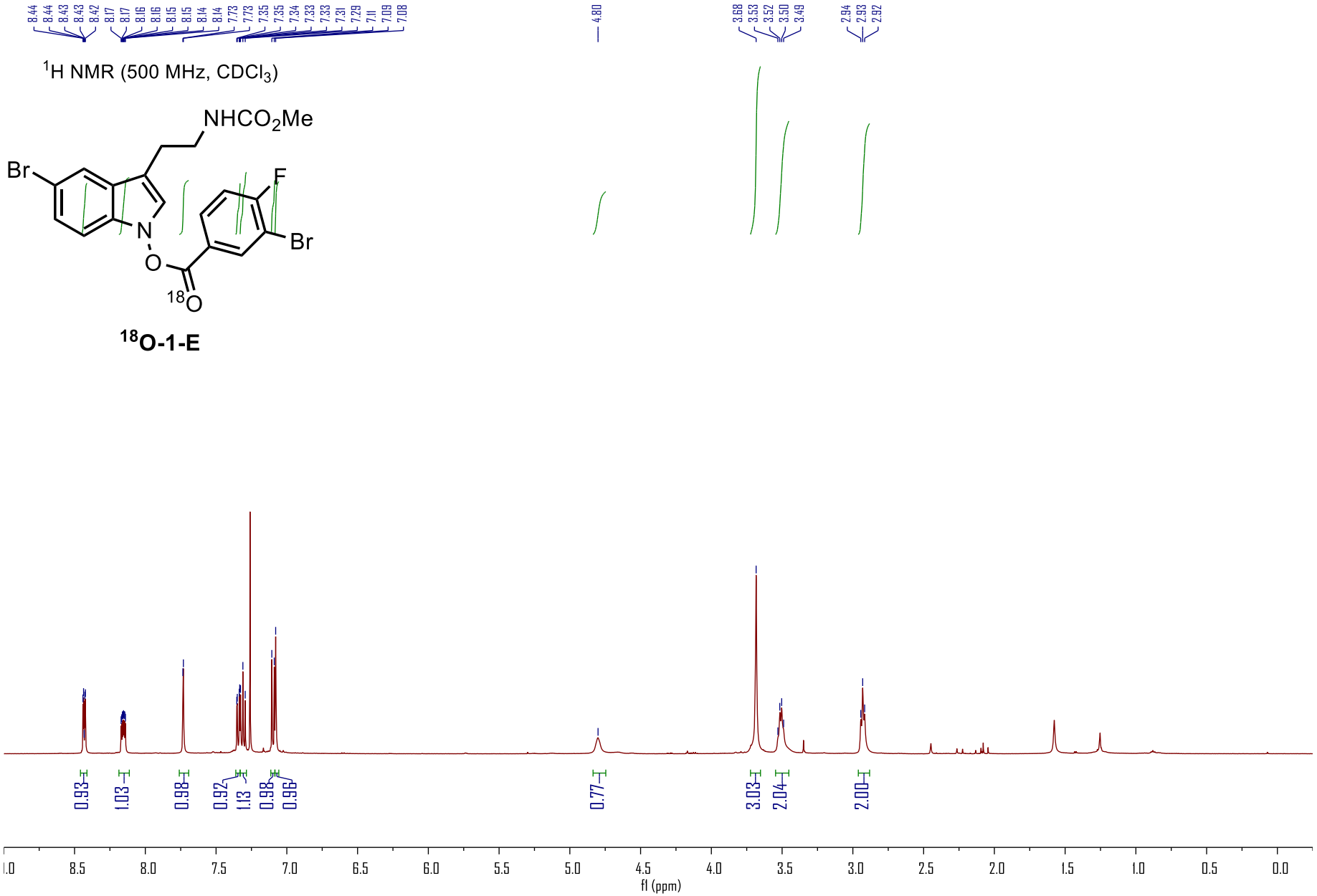

165.4
155.7
154.8
150.0
149.7
133.9
133.6
133.5
129.9
129.5
128.9
128.6
128.3
128.1
111.8
111.7
111.2
110.9
94.0
92.7
80.7
79.9
53.0
52.8
45.5
45.4
38.1
35.9
^{13}C NMR (126 MHz, CDCl$_3$)
Br
^{18}O
NCO$_2$Me
N H
H
^{18}O-2-D
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

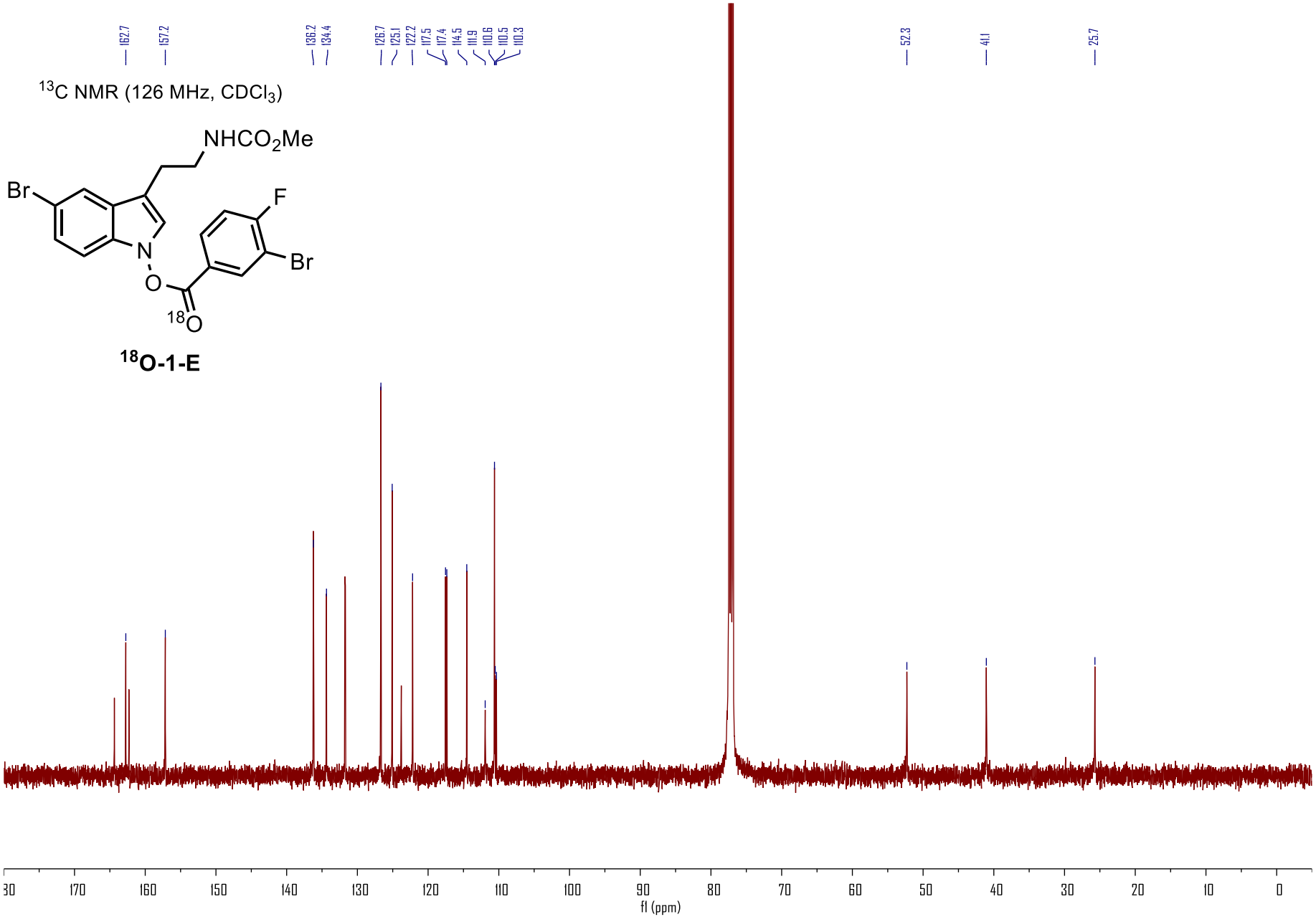

^{1}H NMR (500 MHz, $CDCl_3$)
^{18}O-3-D
7.99 7.97 7.60 7.58 7.56 7.55 7.52 7.44 7.42 7.41 7.28 7.27
6.40 6.38
5.90 5.84
5.21
4.25 4.24 4.23 4.22 4.21 4.12 4.10 4.07 4.03 3.99 3.95 3.93 3.91 3.75 3.74 3.21 3.19 3.17 3.15 3.13 3.12 2.85 2.82 2.76 2.74 2.73 2.68 2.68 2.66 2.64 2.62 1.77 1.75 1.75 1.72
2.00 2.14 2.27 0.77 1.00 0.96 1.01 0.56 2.74 3.08 1.00 1.07 1.00 3.28 3.02
f1 (ppm)


165.2
151.0
133.7
133.5
130.1
129.9
129.1
129.0
128.5
120.7
120.5
109.7
109.5
109.3
93.9
92.9
85.2
84.6
52.9
45.5
45.2
44.8
37.8
25.9
18.2
^{13}C NMR (126 MHz, CDCl$_3$)
O
^{18}O
Br
NCO$_2$Me
N
H
Me
Me
^{18}O-3-D
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

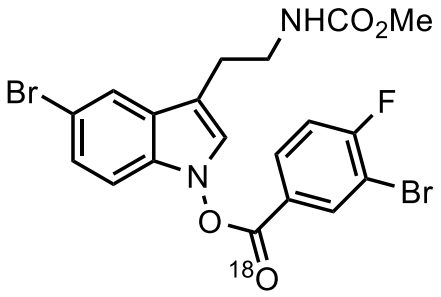

^{1}H NMR (400 MHz, $CDCl_3$)
$H^{18}O$
Br
NCO_2Me
N
H
Me
Me
^{18}O-4-D
7.32 7.32 7.27 7.27
6.36 6.35 6.33
5.39 5.31 5.13 5.09 4.16 4.15 4.14 4.13 4.12 4.12 4.11 4.10 4.10 3.99 3.98 3.96 3.94 3.93 3.91 3.83 3.73 3.22 3.20 3.18 3.17 3.16 3.11
2.35 2.33 2.31 2.29 2.27 2.26 2.25
1.75 1.72
0.94 0.59 0.93 0.54 0.44 0.92 0.62 1.95 0.74 3.09 1.15 2.41 3.13 2.79
f1 (ppm)


149.3
135.7
135.4
133.4
133.3
126.5
126.4
119.9
119.8
109.8
109.5
88.3
87.8
87.1
52.8
45.8
44.8
44.3
38.5
25.9
18.3
^{13}C NMR (101 MHz, CDCl$_3$)
H^{18}O
Br
NCO$_2$Me
N
H
Me
Me
^{18}O-4-D
f1 (ppm)

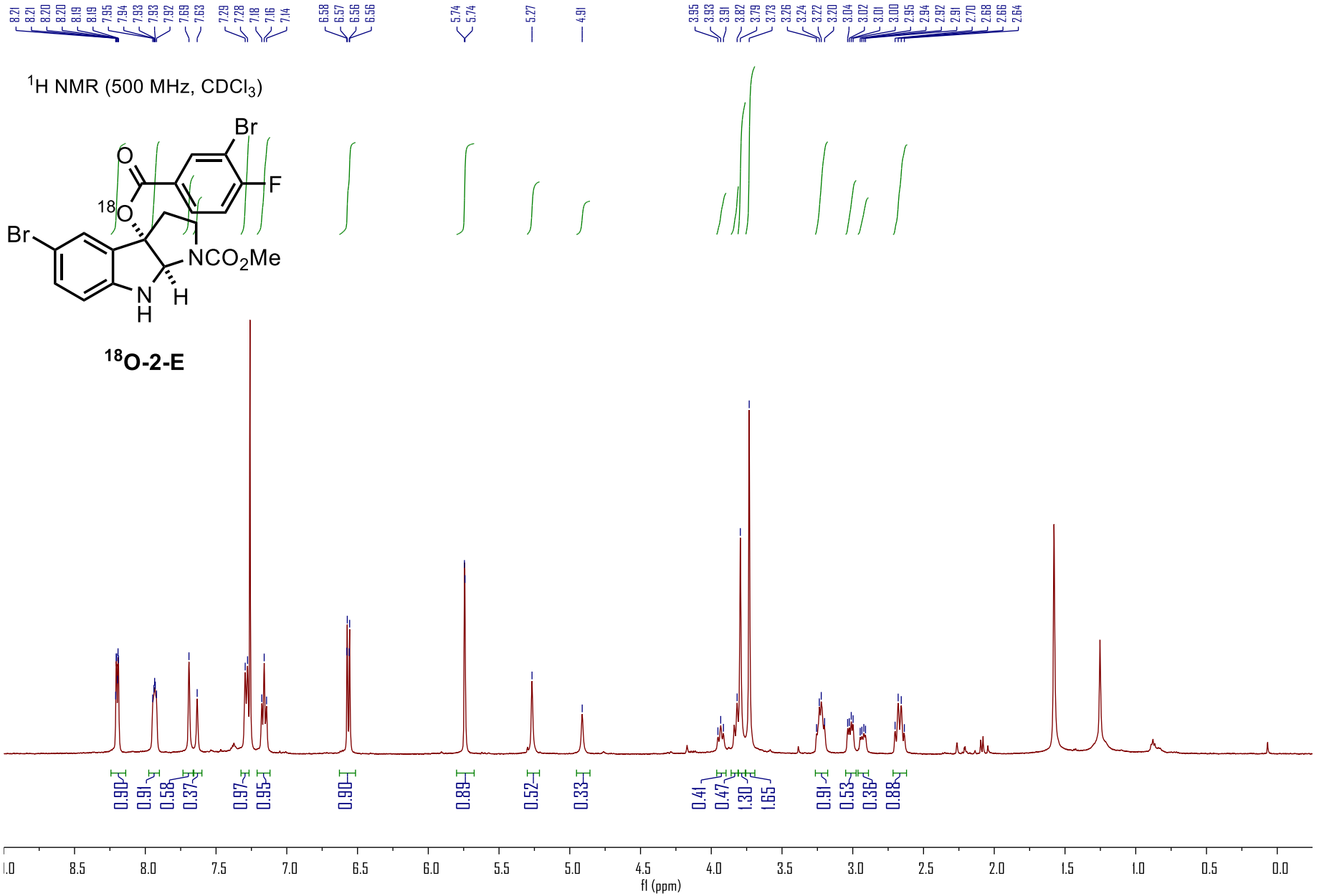

8.44
8.44
8.43
8.43
8.42
8.17
8.17
8.16
8.16
8.15
8.15
8.14
8.14
7.73
7.73
7.35
7.35
7.34
7.33
7.33
7.31
7.29
7.11
7.09
7.08
4.80
3.68
3.53
3.52
3.50
3.49
2.94
2.93
2.92
^{1}H NMR (500 MHz, $CDCl_3$)
$NHCO_2Me$
Br
F
Br
N
O
^{18}O
^{18}O-1-E
0.93
1.03
0.98
0.92
1.13
0.98
0.96
0.77
3.03
2.04
2.00
f1 (ppm)

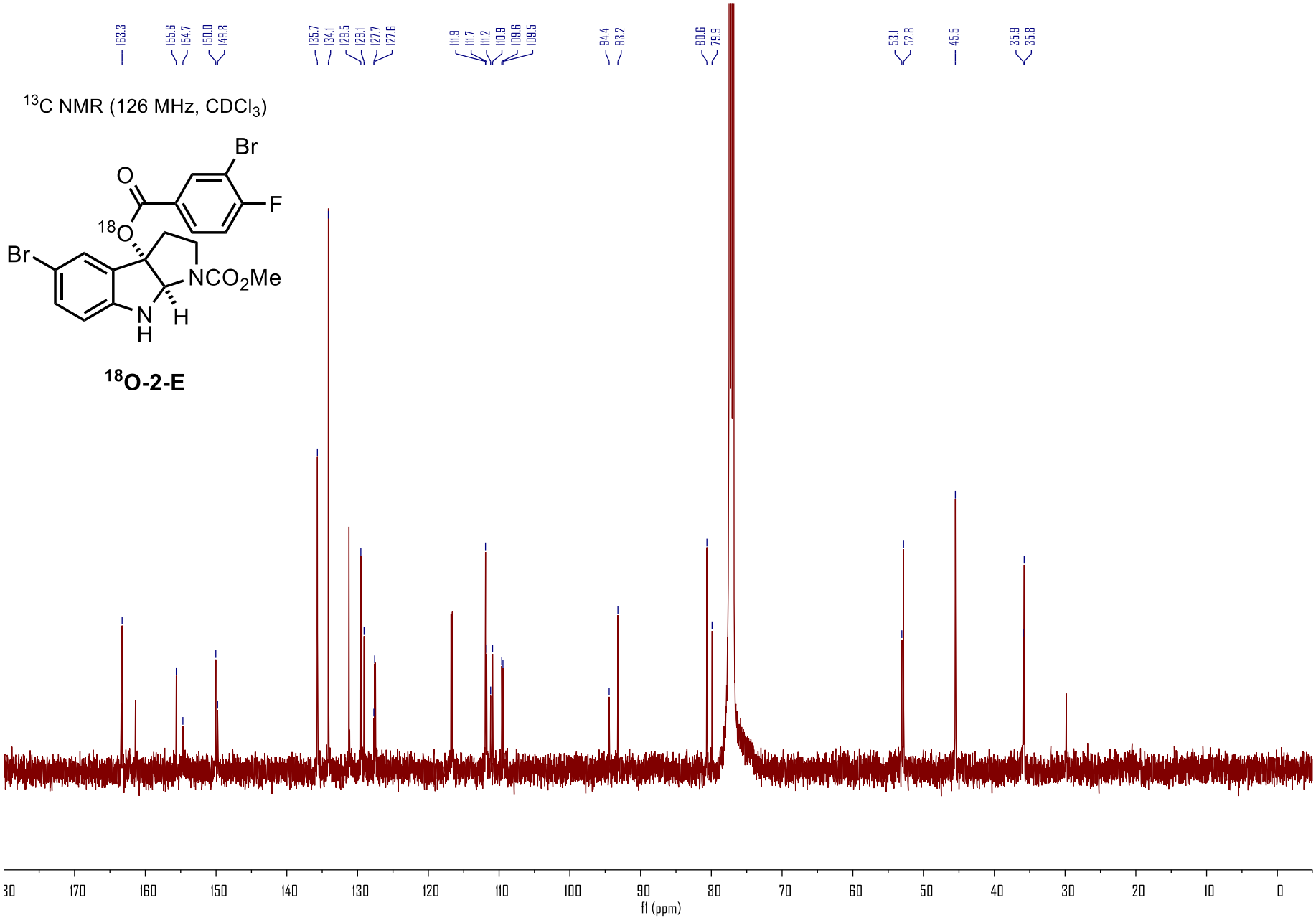

162.7
157.2
136.2
134.4
128.7
125.1
122.2
117.5
117.4
114.5
111.9
110.6
110.5
110.3
52.3
41.1
25.7
^{13}C NMR (126 MHz, CDCl$_3$)
NHCO$_2$Me
Br
F
Br
N
O
^{18}O
^{18}O-1-E
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

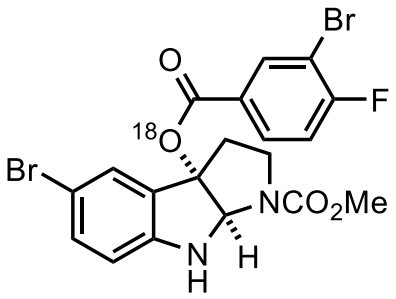


^{18}O-1-E

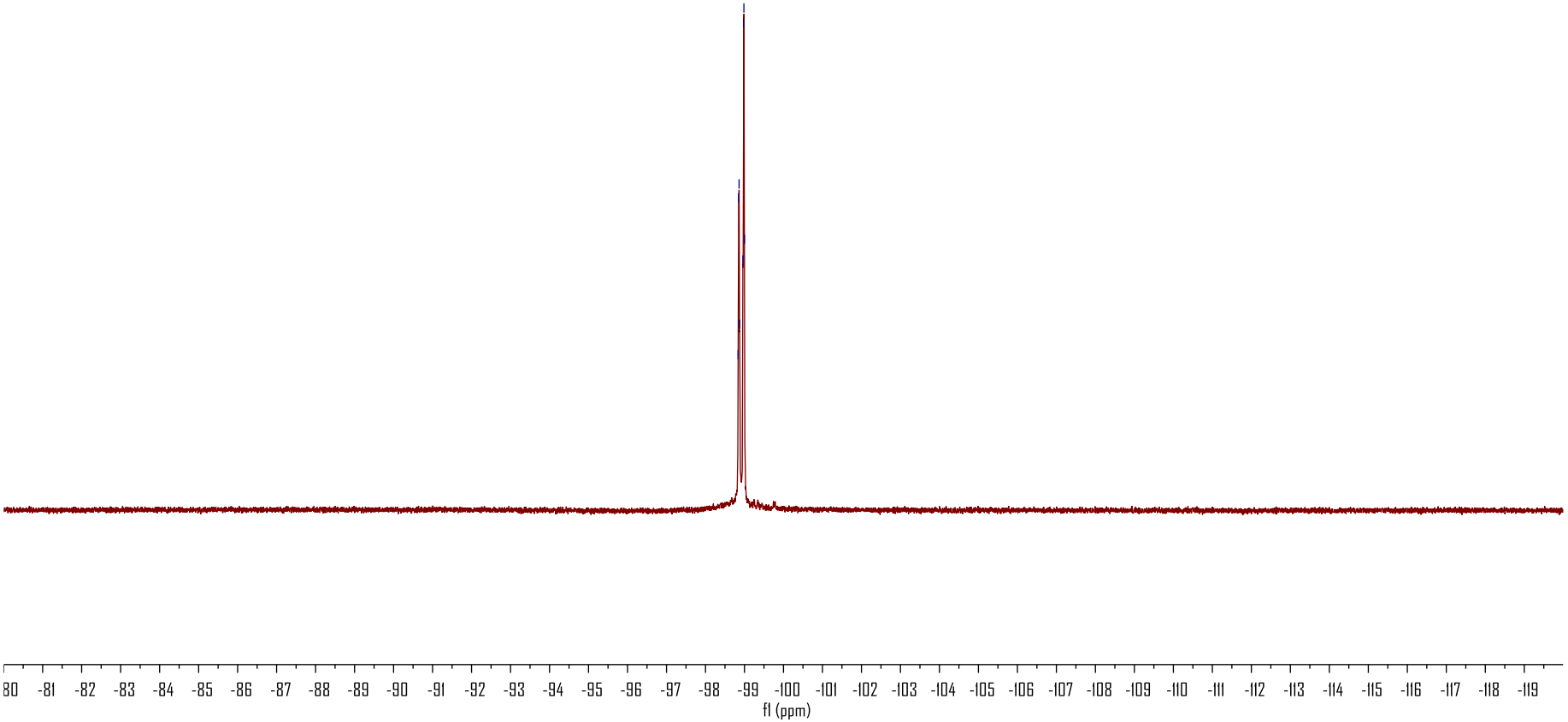

^{1}H NMR (500 MHz, $CDCl_3$)
Br
O
F
^{18}O
Br
NCO_2Me
N
H
H
^{18}O-2-E
8.21
8.21
8.20
8.20
8.19
8.19
7.95
7.94
7.93
7.93
7.92
7.69
7.63
7.29
7.28
7.18
7.16
7.14
6.58
6.57
6.56
6.56
5.74
5.74
5.27
4.91
3.95
3.93
3.91
3.82
3.79
3.73
3.26
3.24
3.22
3.20
3.04
3.02
3.01
3.00
2.95
2.94
2.92
2.91
2.70
2.68
2.66
2.64
0.90
0.91
0.58
0.37
0.97
0.95
0.90
0.89
0.52
0.33
0.41
0.47
1.30
1.65
0.91
0.53
0.36
0.88
f1 (ppm)

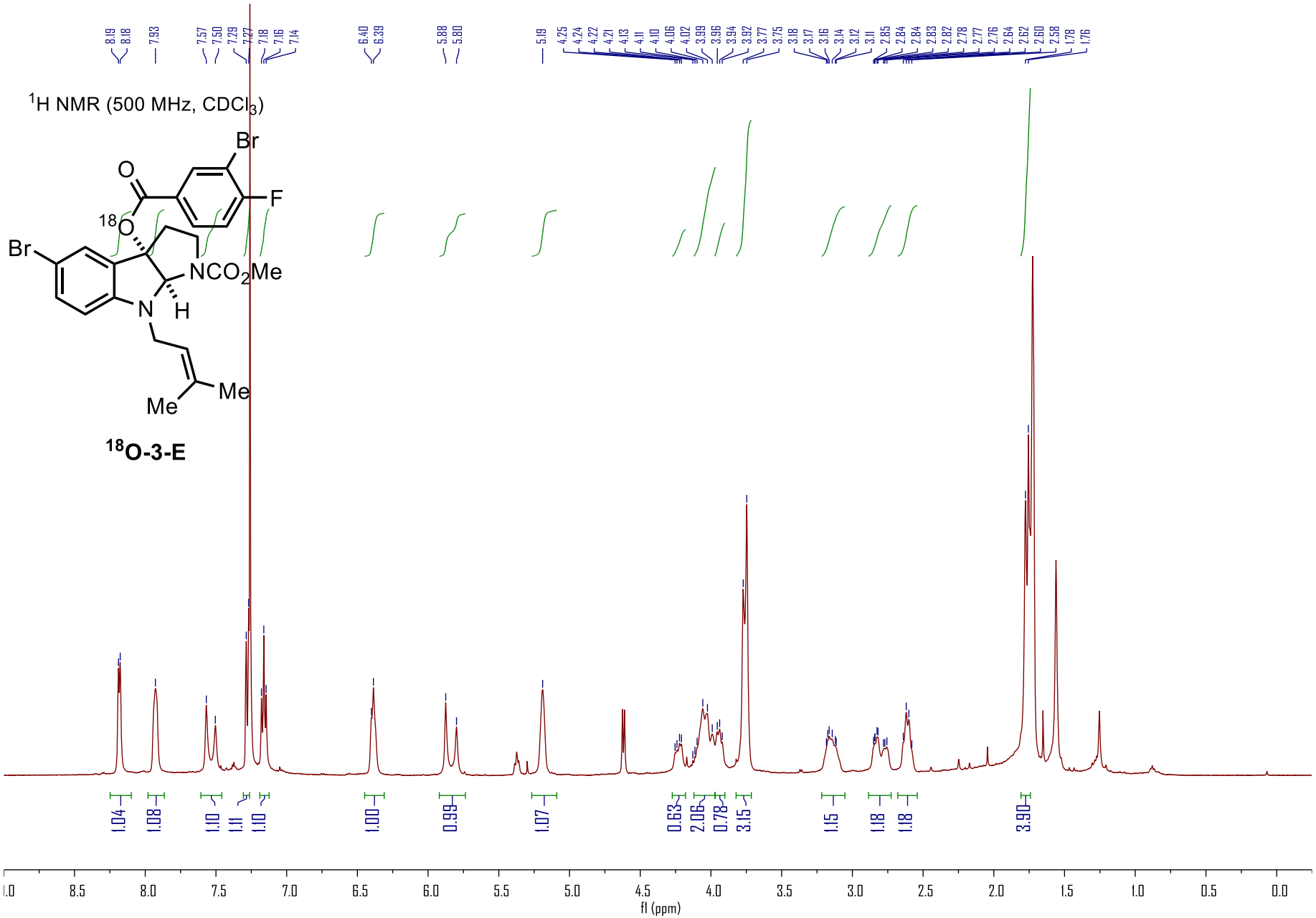

163.3
155.6
154.7
150.0
149.8
135.7
134.1
129.5
128.1
127.7
127.6
111.9
111.7
111.2
110.9
109.6
109.5
94.4
93.2
80.6
79.9
53.1
52.8
45.5
35.9
35.8
^{13}C NMR (126 MHz, CDCl$_3$)
Br
O
F
^{18}O
Br
NCO$_2$Me
N
H
H
^{18}O-2-E
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

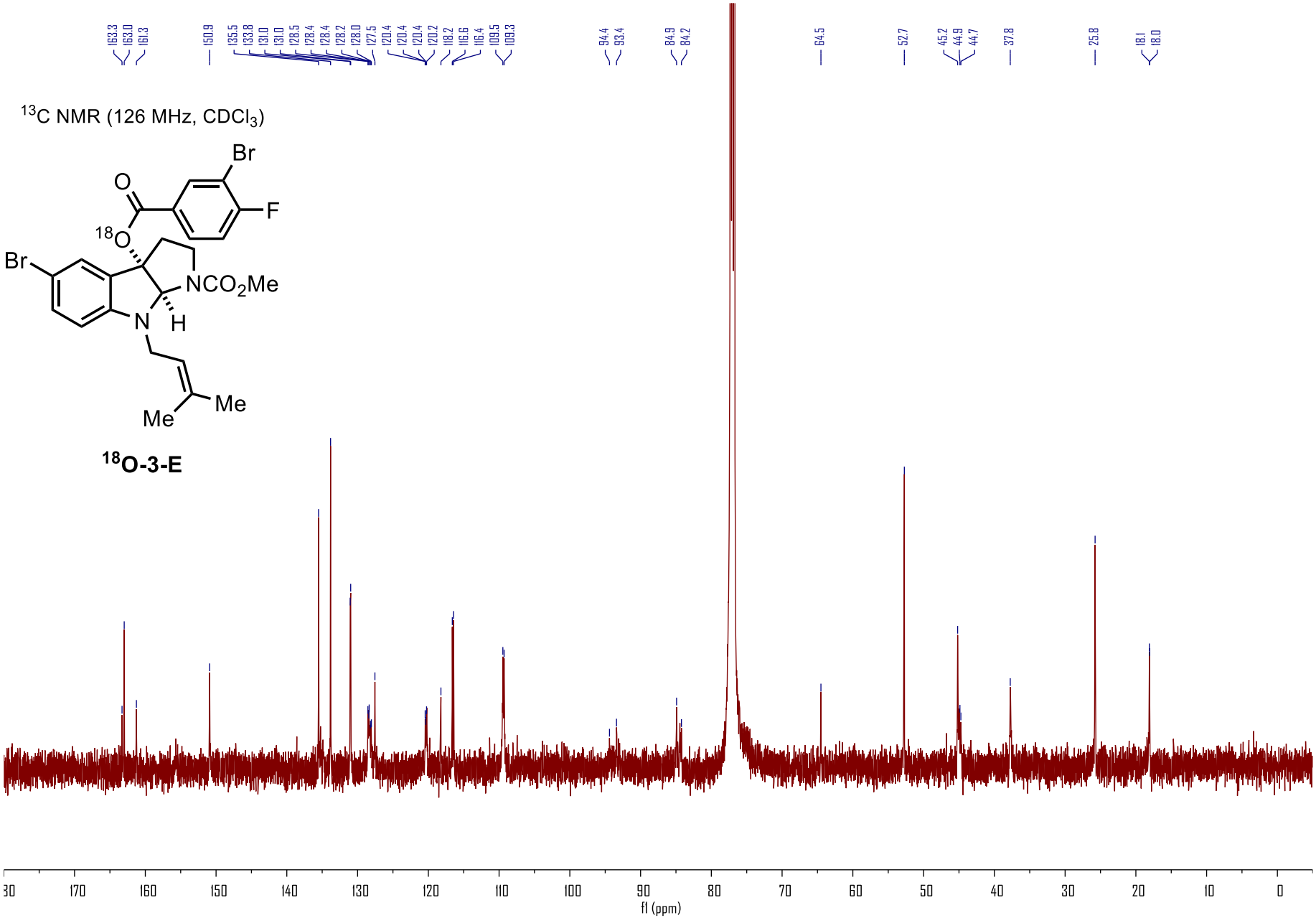
^{19}F NMR (471 MHz, $CDCl_3$)



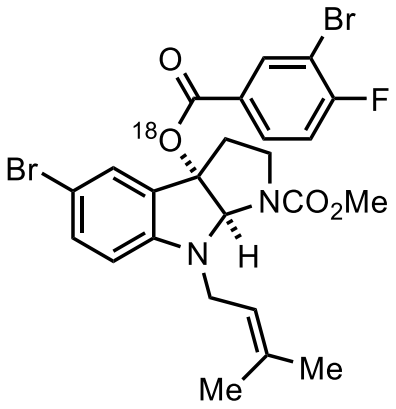
^{18}O-2-E




^{1}H NMR (500 MHz, CDCl$_3$)
^{18}O-3-E
8.19
8.18
7.93
7.57
7.50
7.29
7.27
7.18
7.16
7.14
6.40
6.38
5.88
5.80
5.19
4.25
4.24
4.22
4.21
4.13
4.11
4.10
4.06
4.02
3.99
3.96
3.94
3.92
3.77
3.75
3.18
3.17
3.16
3.14
3.12
3.11
2.85
2.84
2.84
2.83
2.82
2.78
2.77
2.76
2.64
2.62
2.60
2.58
1.78
1.76
1.04
1.08
1.10
1.11
1.10
1.00
0.99
1.07
0.63
2.06
0.78
3.15
1.15
1.18
1.18
3.90
f1 (ppm)

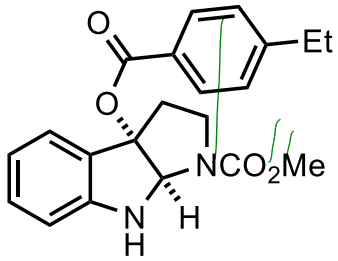

163.3
163.0
161.3
150.9
135.5
133.8
131.0
131.0
128.5
128.4
128.4
128.2
128.0
127.5
120.4
120.4
120.4
120.2
118.2
116.6
116.4
109.5
109.3
94.4
93.4
84.9
84.2
64.5
52.7
45.2
44.9
44.7
37.8
25.8
18.1
18.0
^{13}C NMR (126 MHz, $CDCl_3$)
Br
O
F
^{18}O
Br
NCO_2Me
N
H
Me
Me
^{18}O-3-E
f1 (ppm)

^{19}F NMR (471 MHz, $CDCl_3$)

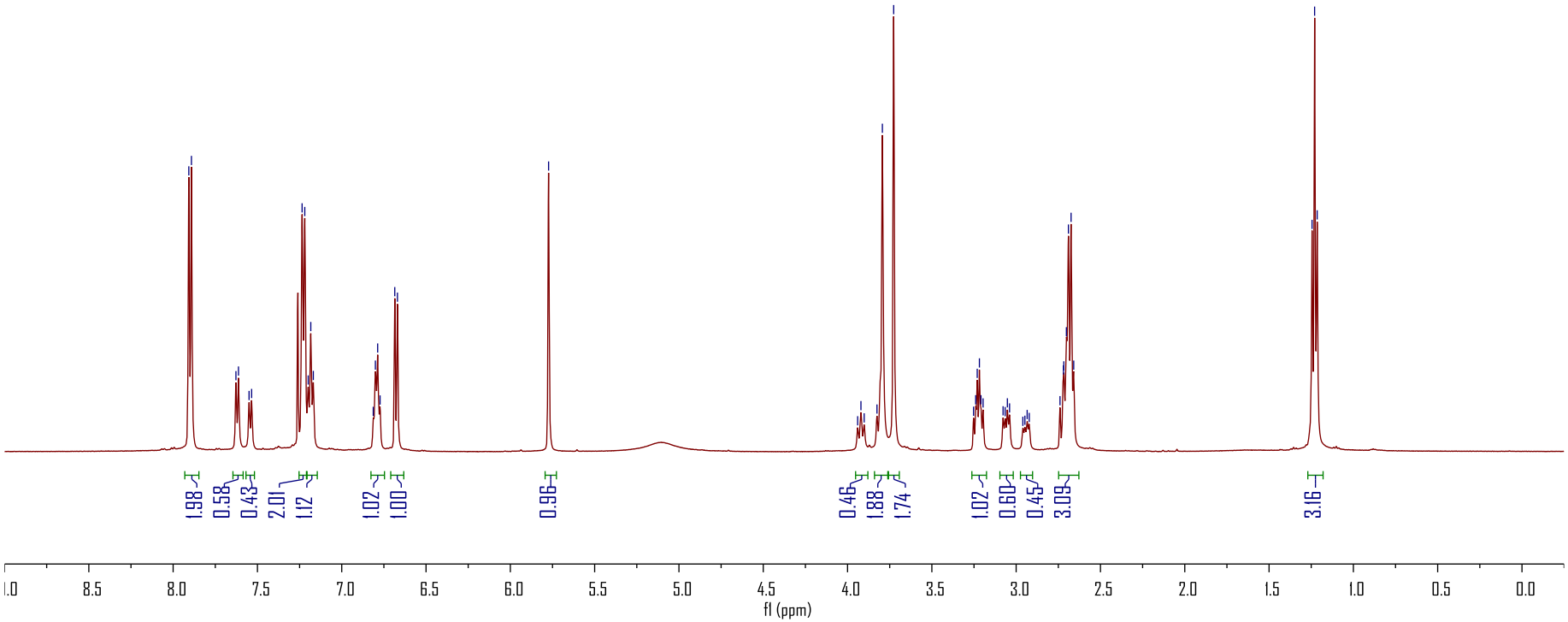


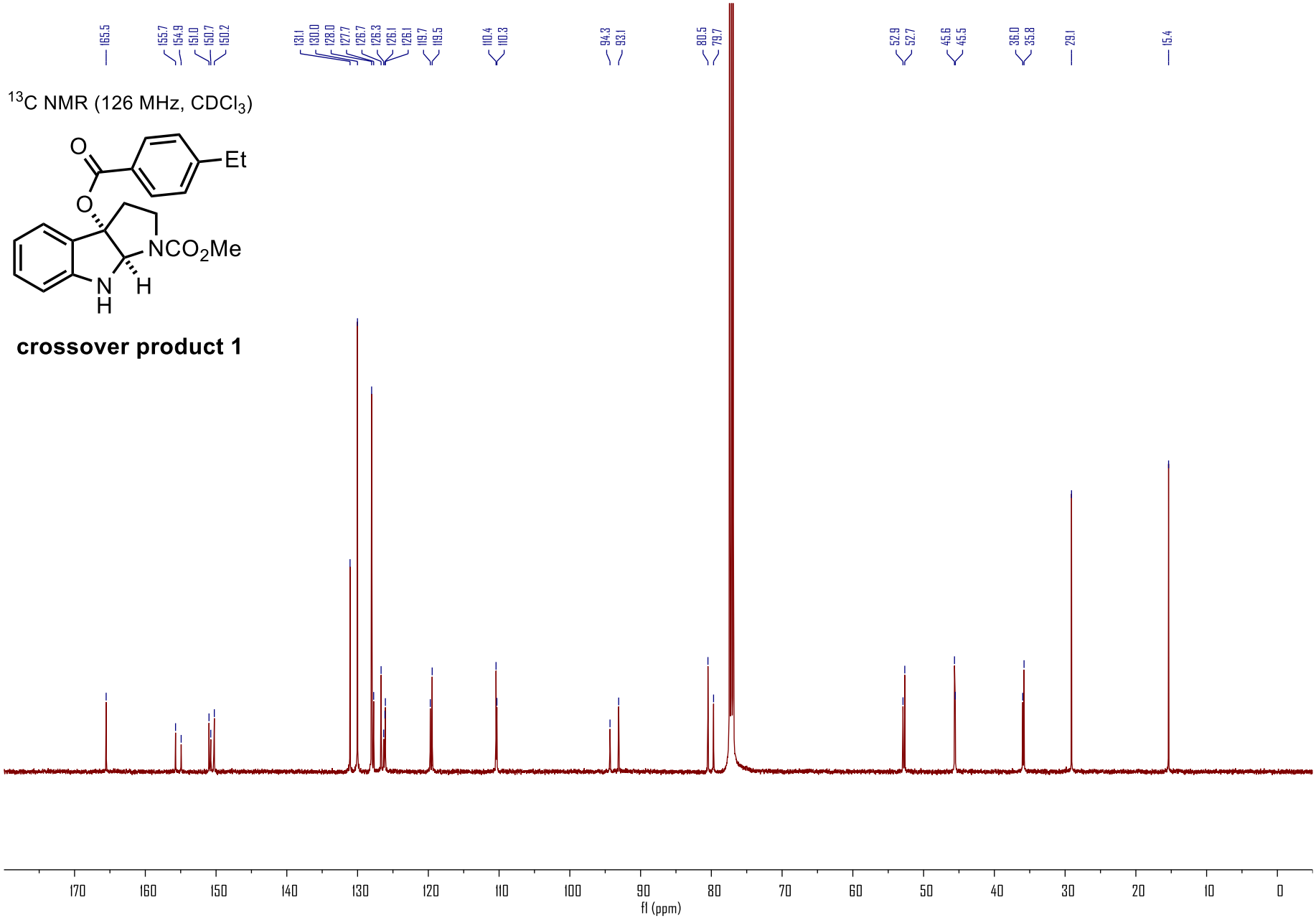
^{18}O-3-E

^{1}H NMR (500 MHz, $CDCl_3$)

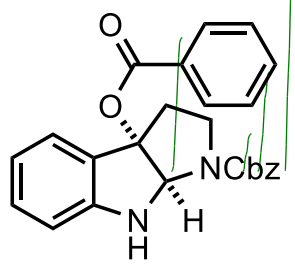


crossover product 1

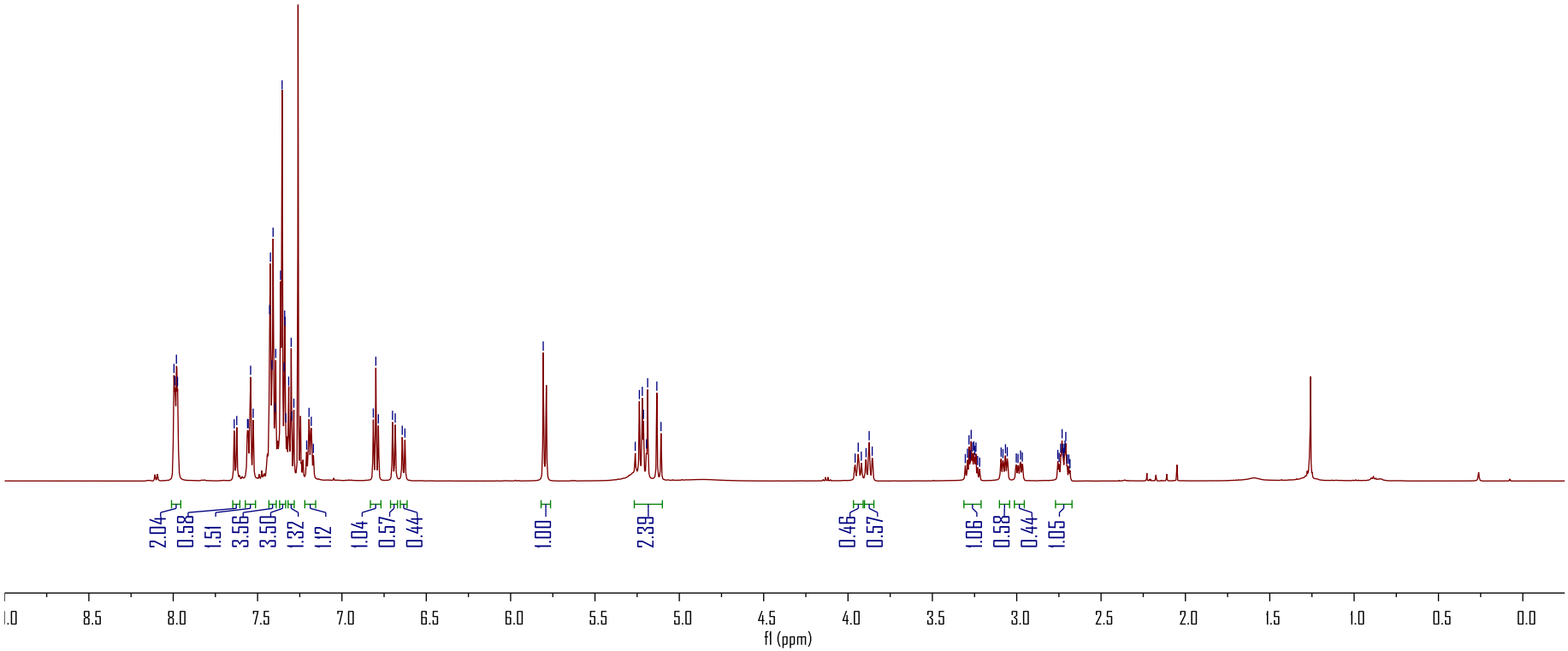


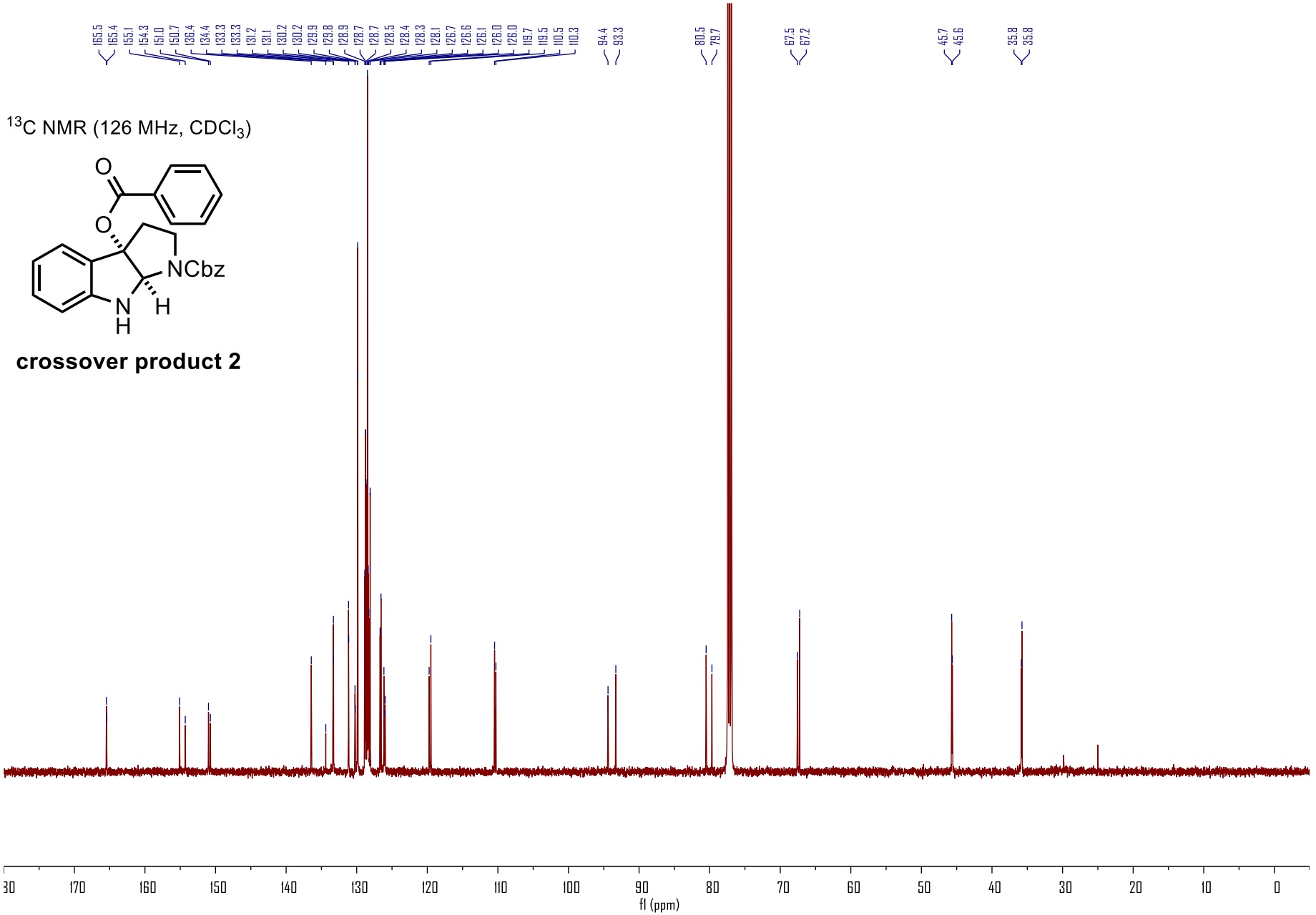

165.5
155.7
154.9
151.0
150.7
150.2
131.1
130.0
128.0
127.7
126.7
126.3
126.1
126.1
119.7
119.5
110.4
110.3
94.3
93.1
80.5
79.7
52.9
52.7
45.6
45.5
36.0
35.8
29.1
15.4
13C NMR (126 MHz, CDCl3)
O
Et
O
NCO2Me
N
H
H
crossover product 1
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR (500 MHz, $CDCl_3$)



crossover product 2




165.5
165.4
155.1
154.3
151.0
150.7
136.4
134.4
133.3
133.3
131.2
131.1
130.2
130.2
129.9
129.8
128.9
128.7
128.7
128.5
128.4
128.3
128.1
126.7
126.6
126.1
126.0
126.0
119.7
119.5
110.5
110.3
94.4
93.3
80.5
79.7
67.5
67.2
45.7
45.6
35.8
35.8
^{13}C NMR (126 MHz, $CDCl_3$)
O
O
NCbz
N
H
H
crossover product 2
f1 (ppm)