Electronic Supplementary Material (ESI) for Faraday Discussions.

Electrochemical Hydrogen Isotope Exchange of Amines Controlled by Alternating Current Frequency

Nibedita Behera,‡[a] Disni Gunasekera,‡[a] Jyoti P. Mahajan,[a] Joseph Frimpong,[a] Zhenfei Liu,[a] and Long Luo*[a]

Contents

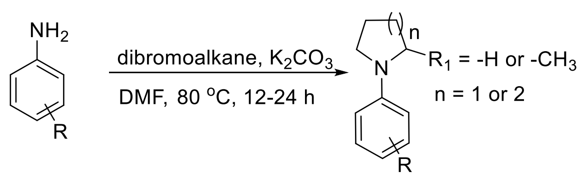
1. General information

All reactions were carried out in oven-dried glassware under a positive pressure of argon using Schlenk line techniques. TLC was performed using pre-coated glass plates with 230-400 mesh silica gel impregnated with a fluorescent indicator (250 nm). Visualization was accomplished using a UV light. Flash chromatography was performed on silica gel flash chromatography columns, Teledyne Isco Combi Flash R_f system utilizing normal phase pre-column cartridges and gold high-performance columns. Purifications were performed using Ethyl acetate: Hexane (v:v) eluting with indicated gradient mixture**.** All proton (^{1}H) nuclear magnetic resonance spectra were recorded on a 400 or 600 MHz spectrometer. All carbon (^{13}C) nuclear magnetic resonance spectra were recorded on a 101 or 151 MHz NMR spectrometer. All fluorine (^{19}F) nuclear magnetic resonance spectra were recorded on a 564 MHz NMR spectrometer. Chemical shifts were expressed in parts per million (δ scale) and were referenced to residual $CDCl_3$ (^{1}H: δ 7.27 ppm, ^{13}C: δ 77.00 ppm). The data are presented as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept= septate, m = multiplet, dd = doublet of doublet, dt = doublet of triplet, td = triplet of doublet), coupling constant in hertz (Hz), number of protons. High-resolution TOF mass spectrometry utilizing electrospray ionization in positive mode or electron ionization was performed to confirm the identity of the new compounds. All AC experiments were carried out using a function generator (RIGOL DG1062) combined with modulated power supply (ACCEL instruments TS200-0A), and glassy carbon (vitreous) plates (100 mm × 100 mm) were purchased from SPI Supplies. DC experiments were carried out using an IKA ElectraSyn 2.0. The discharge voltage, frequency, and waveform were monitored using an oscilloscope (SIGLENT Technologies SDS1202X-E). Voltammetry experiments were carried out using a CHI 650E potentiostat. All the mass spectra were recorded on a Thermo LTQ-Orbitrap spectrometry utilizing electrospray ionization in positive mode.

2. General experimental procedures for substrates synthesis

2A. N-aryl pyrrolidines/piperidines

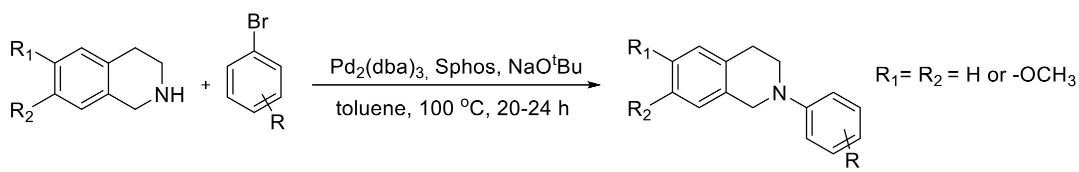
Compounds **2** and **14-24** were synthesized using the following procedure.



According to a literature procedure,[1] potassium carbonate (K_2CO_3) (30 mmol, 1.2 equiv.), appropriate aniline (25 mmol, 1 equiv.), and anhydrous *N, N*- dimethylformamide (DMF) (30 mL) was added in an oven-dried two-neck round-bottom flask under argon atmosphere. The resulting suspension was stirred for 5 min, and appropriate dibromoalkane (30 mmol, 1.2 equiv.) was added. The reaction mixture was heated to 80˚C for 12-24 h. After completion, the reaction mixture was cooled to room temperature and diluted with ice-cold water (100 mL). The aqueous layer was extracted with ethyl acetate (100 mL x 2), and the separated organic layer was washed with brine (50 mL) and dried over sodium sulfate. The organic layer was concentrated in *vacuo,* and the resulting crude product was purified using flash silica gel column chromatography to afford *N*-aryl pyrrolidines. All synthesized substrates are known compounds, and their analytical data were consistent with that reported in the literature.[2-6]

2B. N-aryl tetrahydroisoquinolines

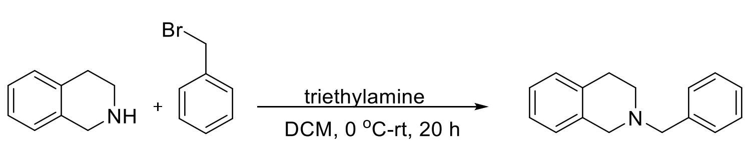
Compounds **3-13** were synthesized according to the following procedure.



According to a literature procedure,[7] an oven-dried pressure tube equipped with a stir bar was charged with $Pd_2(dba)_3$ (3 mol %), Sphos (8 mol%), and anhydrous toluene (5 mL) under argon atmosphere. The resulting mixture was stirred for a minute, and bromoarene (2.5 mmol, 1 equiv.), tetrahydroisoquinoline (3 mmol, 1.2 equiv.), and NaO^tBu (3.5 mmol, 1.4 equiv.) were added. The pressure tube was sealed using a Teflon cap under the stream of argon and heated to 100 °C for 20-24 h. After completion, the reaction mixture was cooled to room temperature and quenched by adding water (20 mL). The aqueous layer was extracted using ethyl acetate (20 mL x 2). The combined organic layer was washed with brine (50 mL), dried over sodium sulfate, and concentrated under reduced pressure to obtain the crude product. The obtained crude product was purified using flash silica-gel column chromatography to afford the *N*-aryl tetrahydroisoquinolines. All synthesized substrates are known compounds, and their analytical data were consistent with that reported in the literature [8-9].

2C. N-benzyl tetrahydroisoquinoline

Compound **1** was synthesized according to the following procedure.



According to a literature procedure,[10] an oven-dried two-neck round-bottom flask was charged with tetrahydroisoquinoline (10 mmol, 1 equiv.), triethylamine (30 mmol, 3 equiv.), and anhydrous dichloromethane (20 mL) using syringe under argon atmosphere. The resulting suspension was cooled to 0 °C (ice bath), and benzyl bromide

(15 mmol, 1.5 equiv.) was added dropwise. The reaction mixture was stirred for 20 h. After completion, the reaction mixture was filtered, and the organic layer was washed with brine (20 mL). The separated organic layer was dried over sodium sulfate, and the solvent was evaporated under a vacuum resulting mixture was purified using flash silica-gel column chromatography to obtain *N*-benzyl tetrahydroisoquinoline.

3. Experimental setups for electrochemical HIE reactions and voltammetric measurements.

Fig. S1. Photographs of the experimental setup for DC electrolysis using a commercial IKA ElectraSyn 2.0.

Fig. S2. Photographs of the experimental setup for AC electrolysis consisting of a TS200 amplifier from Accel Instruments and RIGOL DG1062 waveform generator, a Schlenk tube, and two glassy carbon electrodes.

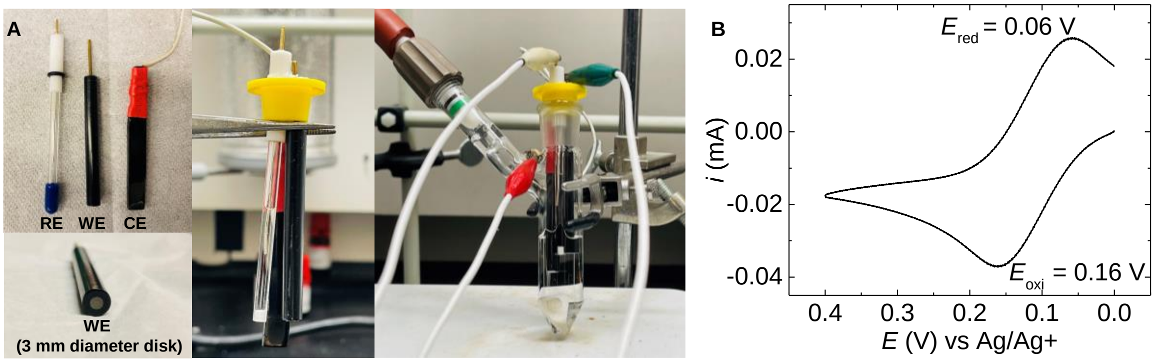


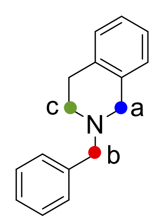
Fig. S3. (A) Photographs of the three-electrode setup for electrochemical measurements. A 3-mm-diameter glassy carbon disk electrode as the working electrode (WE), a glassy carbon plate as the counter electrode (CE), and an Ag/Ag^+ as the reference electrode (RE). The Ag/Ag^+ electrode was prepared by filling the glass tube with 10 mM $AgNO_3$ and $LiClO_4$ (0.1 M, supporting electrolyte) in an anhydrous DMA solution. (B) Cyclic voltammogram of ferrocene in anhydrous DMA containing 0.1 M $LiClO_4$. Scan rate = 0.1 V/s. The Ag/Ag+ reference electrode potential was calibrated using ferrocene/ferrocenium ($E_{Fc/Fc+}$ =0.11 vs. Ag/Ag^+).

4. *iR* correction

Due to the *iR* drop associated with the charging and discharging of the electrical double layer during AC electrolysis, the actual voltage available for electrochemical reactions (V_{ec}) is lower than the amplitude of the applied AC waveform (V_{peak}) with a frequency of 1/2*t*, as estimated by the following equation:[11]

$V_{ec} = V_{peak}\,(1- \exp(-2t/R_{electrolyte}C_{EDL}))$, where $R_{electrolyte}$ and C_{EDL} were the solution resistance and electrical double-layer capacitance of the AC electrolysis setup, respectively. $R_{electrolyte}$ and C_{EDL} were measured to be 14.7 Ω and 0.15 mF using previously reported electrochemical techniques.[12] V_{ec} is the potential difference between the peak potentials for amine oxidation and methyl thioglycolate reduction in their cyclic voltammograms. For **1** and **2**, V_{ec} was 3.5 V and 3.1 V, respectively, according to **Fig. 1B-C**.

5. Determining the relative k_{HAT}



The HAT kinetics is correlated with the BDE of α-amino C-H bond following the Evans-Polanyi principle. More specifically, $\Delta G^‡ = 0.47 \times \Delta BDE$,[13] where ΔBDE is the BDE difference between two α-amino C-H bonds and $\Delta G^‡$ is the activation energy barrier difference for HAT at the two sites. Taking **1** as the example, the BDEs of C-H bonds at sites **a** and **b** are 77.0 kcal/mol and 82.3 kcal/mol, respectively. Thus, $\Delta G^‡ = 0.47 \times (82.3\text{-}77.0)$ kcal/mol = 2.65 kcal/mol. The relative HAT kinetics for **a** and **b** (k_a/k_b) are calculated from $\Delta G^‡$ using the Arrhenius equation,

$$\frac{k_a}{k_b} = e^{-\frac{\Delta G^{\ddagger}}{RT}} = 0.011$$

Where R is the universal gas constant (8.314 J/(mol·K)), T is 298 K.

6. Determining the relative k_{PT}

Relative deprotonation kinetics for **1** and **2** were estimated using a voltammetric method previously developed by our group.[12] Briefly, we varied the scan rate and compared the cyclic voltammograms of an amine with and without base (NaOAc was used as the base in **Fig. S4**). From the scan rates at which $i_0 \approx i_1$ for **1** (200 V/s) and **2** (5 V/s), we can estimate the relative deprotonation kinetics to be 20 : 1. Note that we assume that the relative deprotonation kinetics does not significantly vary as the base changes from NaOAc used in the voltammetric study to thiolate used in our electrochemical HIE reactions.

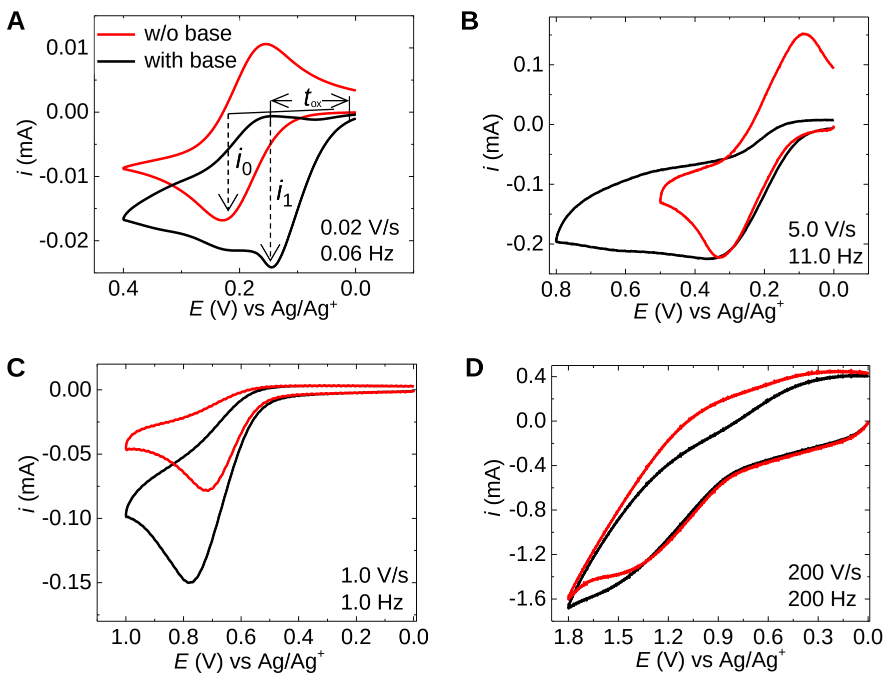


Fig. S4. (A), (B) Cyclic voltammograms of **2** (2mM) in the presence (black curve) and absence (red curve) of NaOAc in anhydrous DMA containing $LiClO_4$ (0.1 M) at the scan rate of 0.02 V/s and 5.0 V/s respectively. (C), (D) Cyclic voltammograms of **1** (2mM) in the presence (black curve) and absence (red curve) of NaOAc in anhydrous DMA containing $LiClO_4$ (0.1 M) at the scan rate of 1.0 V/s and 200 V/s respectively.

7. Determining the equivalent AC frequency for the DC electrolysis conditions:

We first calculated the diffusion coefficients (*D*) of **1** (4.34×10^{-6} cm^2/s) and **2** (8.49×10^{-6} cm^2/s) from their cyclic voltammograms at different scan rates (v) using the Randles - Sevcik equation,[14]

$$i_p = 0.4463\, n^{3/2}\, F^{3/2}\, A\, \frac{D^{1/2} c\, v^{1/2}}{(RT)^{1/2}}$$

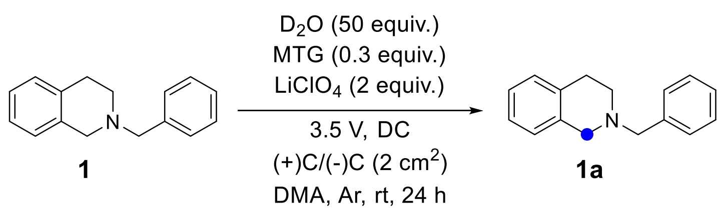
where i_p is the peak current in the voltammogram, n is the number of electrons transferred in the redox event (= 1), F is Faraday constant (96485 C/mol), A is working electrode surface area, c is concentration, R is the universal gas constant (8.314 J/mol K), and T is 298 K. Then, the diffusion time (t) between the two electrodes with a separation distance of d can be estimated by the following diffusion equation:

$$d = (2Dt)^{1/2}$$

For the IKA setup with d = 5 mm, $t = 2.9 \times 10^4$ s or an equivalent $f = 3.5 \times 10^{-5}$ Hz for **1** and 6.8×10^{-5} Hz for **2**. Similarly, for our home-built setup with d= 1 mm, $f = 8.7 \times 10^{-4}$ Hz for **1** and 1.7×10^{-3} Hz for **2**.

8. Reaction optimization for **1** and **2**

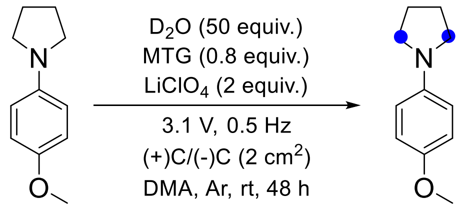
Table S1. Optimization table for **1**



Entry	Variation from the standard conditions	D-incorporation %
1	None	60
2	$(i\text{-Pr})_3$SiSH*	54
3	No thiol	00
4	No voltage	00

Reaction scale: 0.25 mmol **1**, 12.5 mmol D_2O, 0.5 mmol $LiClO_4$, 4 mL DMA, Ar, constant voltage, 24 h, D-incorporation from ^1H NMR. * voltage amplitude = 3

Table S2. Optimization table for **2**



Entry	Variation from the standard conditions	D-incorporation (%)
01	None	89
02	No voltage	00
03	No thiol	00
04	0.3 eq MTG	60
05	0.5 eq MTG	50
06	1.0 eq MTG	88
07	1.2 eq MTG	81
08	0.3 eq (*i*-Pr)$_3$SiSH as thiol	07
09	NMP as the solvent (24 h)	12
10	2 eq NaOAc as the base	50
11	36 h	71
12	30 eq D_2O (0.3 eq MTG)	52

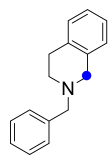
Reaction scale: 0.25 mmol **2**, 12.5 mmol D_2O, 0.2 mmol MTG, 0.5 mmol $LiClO_4$, 4 mL DMA, Ar, constant voltage = 3.1 V, 48 h, D-incorporation from ^1H NMR.

Reproducibility of HIE reaction:

The HIE reactions of both **1** and **2** were repeated four times. The D-incorporation and yield for **1a** are 58-60% and 42-45%, respectively. In the case of **2a**, the D-incorporation and yield are 86-89% and 40-44%, respectively. Hence, these results confirmed the reproducibility of these HIE reactions.

9. Experimental details and characterization data

2-benzyl-1,2,3,4-tetrahydroisoquinoline (**1**, **1a**)

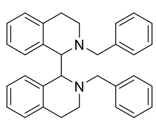


1a

1: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.46 – 7.42 (m, 2H), 7.40 – 7.35 (m, 2H), 7.32 – 7.29 (m, 1H), 7.16 – 7.14 (m, 3H), 7.02 (d, *J* = 5.4 Hz, 1H), 3.73 (s, 2H), 3.68 (s, 2H), 2.94 (d, *J* = 4.1 Hz, 2H), 2.79 (dd, *J* = 9.4, 5.6 Hz, 2H).

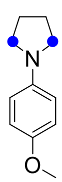
1a: **Reaction condition: DC**: 3.5 V; 24 h, 25 mg, 45% yield, 60 D%. The crude product was purified using flash silica-gel column chromatography to afford **1a** as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.3 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.32-7.29 (m, 1H), 7.17 – 7.09 (m, 3H), 7.02 – 6.98 (m, 1H), 3.76 (s, 2H), 3.71 – 3.66 (m, 0.77H), 2.95 (t, *J* = 5.9 Hz, 2H), 2.83 (t, *J* = 5.6 Hz, 2H). Deuterium incorporation of **1a** determined by liquid chromatography-mass spectrometry (LCMS)/IsoPat2 analysis[15]: 79% D (raw data and its fitting results are provided in Appendix B).

2,2'-dibenzyl-1,1',2,2',3,3',4,4'-octahydro-1,1'-biisoquinoline (**Dimer**)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.4 Hz, 2H), 7.37 – 7.31 (m, 8H), 7.29 – 7.26 (m, 2H), 7.02 – 6.91 (m, 6H), 4.20 (s, 2H), 4.07 (d, *J* = 13.2 Hz, 2H), 3.54 (d, *J* = 13.2 Hz, 2H), 3.32 – 3.25 (m, 2H), 2.75 – 2.67 (m, 2H), 2.64 – 2.56 (m, 2H), 2.54 – 2.48 (m, 2H).

1-(4-methoxyphenyl)pyrrolidine (2, 2a)

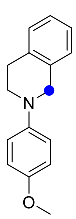


2a

2: **^{1}H NMR** (600 MHz, CDCl3) δ 6.91 – 6.83 (m, 2H), 6.59 – 6.54 (m, 2H), 3.79 (s, 3H), 3.25 (d, *J* = 6.3 Hz, 4H), 2.04 – 1.99 (m, 4H).

2a: Reaction condition: **AC**: 0.5 Hz, 3.1 V (peak amplitude); 48 h, 18 mg, 40% yield, 89% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **2a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 6.89 – 6.83 (m, 2H), 6.56 (d, *J* = 8.5 Hz, 2H), 3.77 (s, 3H), 3.23 (s, 0.44H), 1.99 (d, *J* = 4.2 Hz, 4H). Deuterium incorporation of 2**a**: 85% D (mass).

2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (3, 3a)



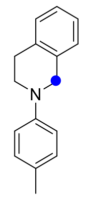
3a

3: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.11 (m, 4H), 7.00 (d, *J* = 9.0 Hz, 2H), 6.90 – 6.87 (m, 2H), 4.32 (s, 2H), 3.80 (s, 3H), 3.47 (t, *J* = 5.9 Hz, 2H), 3.01 (t, *J* = 5.8 Hz, 2H).

3a: **Reaction condition: DC**: 3.2 V; 24 h, 36 mg, 60% yield, 93 D%. The crude product was purified using flash silica-gel column chromatography to afford **3a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20 –

7.14 (m, 4H), 7.02 – 6.98 (m, 2H), 6.91 – 6.87 (m, 2H), 4.32 – 4.29 (m, 0.14H), 3.80 (s, 3H), 3.47 (t, J = 5.9 Hz, 2H), 3.00 (t, J = 5.9 Hz, 2H). Deuterium incorporation of 3**a**: 97% D (mass).

2-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline (4, 4a)

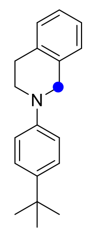


4a

4: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20 – 7.14 (m, 4H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 8.5 Hz, 2H), 4.37 (s, 2H), 3.53 (t, *J* = 5.9 Hz, 2H), 3.00 (t, *J* = 5.8 Hz, 2H), 2.29 (s, 3H).

4a: **Reaction condition: DC**: 3.3 V; 18 h, 17 mg, 30% yield, 70 D%. The crude product was purified using flash silica-gel column chromatography to afford **4a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20 – 7.14 (m, 4H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 8.3 Hz, 2H), 4.36 (d, *J* = 11.0 Hz, 0.63H), 3.57 – 3.48 (m, 2H), 3.00 (t, *J* = 5.8 Hz, 2H), 2.30 (s, 3H). Deuterium incorporation of **4a**: 38% D (mass).

2-(4-(tert-butyl)phenyl)-1,2,3,4-tetrahydroisoquinoline (5, 5a)

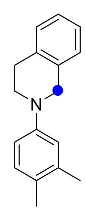


5a

5: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.34 (d, *J* = 8.9 Hz, 2H), 7.22 – 7.15 (m, 4H), 6.97 (d, *J* = 8.8 Hz, 2H), 4.41 (s, 2H), 3.56 (t, *J* = 5.8 Hz, 2H), 3.01 (t, *J* = 5.8 Hz, 2H), 1.33 (s, 9H).

5a: **Reaction condition: DC**: 3.3 V; 24 h, 7 mg, 10% yield, 86 D%. The crude product was purified using flash silica-gel column chromatography to afford **5a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H), 7.22 – 7.14 (m, 4H), 6.96 (d, *J* = 8.7 Hz, 2H), 4.40 – 4.37 (m, 0.26H), 3.55 (t, *J* = 5.8 Hz, 2H), 2.99 (t, *J* = 5.8 Hz, 2H), 1.31 (s, 9H). Deuterium incorporation of **5a**: 87% D (mass).

2-(3,4-dimethylphenyl)-1,2,3,4-tetrahydroisoquinoline (6, 6a)

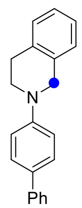


6a

6: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20 – 7.14 (m, 4H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.85 (s, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 4.37 (s, 2H), 3.52 (t, *J* = 5.8 Hz, 2H), 3.00 (t, *J* = 5.7 Hz, 2H), 2.27 (s, 3H), 2.21 (s, 3H).

6a: **DC**: 3.2 V; 24 h, 24 mg, 40% yield, 90 D%. The crude product was purified using flash silica-gel column chromatography to afford **6a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20-7.15 (m, 4H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.84 (s, 1H), 6.78 (dd, *J* = 8.2, 2.3 Hz, 1H), 4.34 (s, 0.23H), 3.52 (t, *J* = 5.9 Hz, 2H), 3.00 (t, *J* = 5.8 Hz, 2H), 2.27 (s, 3H), 2.21 (s, 3H). Deuterium incorporation of **6a**: 90 %D (mass).

2-([1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydroisoquinoline (7, 7a)

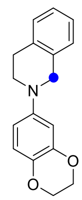


7a

7: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (t, *J* = 8.6 Hz, 4H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.24 – 7.16 (m, 4H), 7.07 (d, *J* = 8.6 Hz, 2H), 4.49 (s, 2H), 3.64 (t, *J* = 5.9 Hz, 2H), 3.03 (t, *J* = 5.8 Hz, 2H).

7a: **Reaction condition: DC**: 3.3 V; 36 h, 6 mg, 8% yield, 88 D%. The crude product was purified using flash silica-gel column chromatography to afford **7a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (t, *J* = 8.6 Hz, 4H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.23 – 7.18 (m, 4H), 7.06 (d, *J* = 8.6 Hz, 2H), 4.49 – 4.46 (m, 0.24H), 3.64 (t, *J* = 5.9 Hz, 2H), 3.03 (t, *J* = 5.9 Hz, 2H). Deuterium incorporation of **7a**: 85% D (mass).

2-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1,2,3,4-tetrahydroisoquinoline (8, 8a)

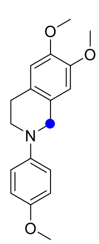


8a

8: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 – 7.12 (m, 4H), 6.82 – 6.80 (m, 1H), 6.56 (s, 2H), 4.30 (s, 2H), 4.28 – 4.25 (m, 2H), 4.24 – 4.21 (m, 2H), 3.45 (t, *J* = 5.8 Hz, 2H), 2.98 (t, *J* = 5.7 Hz, 2H).

8a: **Reaction condition: DC**: 3.2 V; 24 h, 17 mg, 25% yield, 84 D%. The crude product was purified using flash silica-gel column chromatography to afford **8a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 – 7.10 (m, 4H), 6.85 – 6.78 (m, 1H), 6.57 – 6.54 (m, 2H), 4.34 (d, *J* = 25.2 Hz, 0.17H), 4.28 – 4.25 (m, 2H), 4.24 – 4.21 (m, 2H), 3.46 (t, *J* = 5.9 Hz, 2H), 2.98 (t, *J* = 5.9 Hz, 2H). Deuterium incorporation of **8a**: 79% D (mass).

6,7-dimethoxy-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (9, 9a)

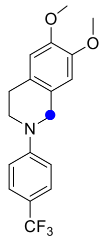


9a

9: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.00 (s, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 6.64 (d, *J* = 7.1 Hz, 2H), 4.24 (s, 2H), 3.88 (d, *J* = 3.0 Hz, 6H), 3.79 (s, 3H), 3.45 (t, *J* = 5.2 Hz, 2H), 2.91 (s, 2H).

9a: **Reaction condition: DC**: 3.2 V; 24 h, 45 mg, 60% yield, 93 D%. The crude product was purified using flash silica-gel column chromatography to afford **9a** as a white solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.00 – 6.98 (m, 2H), 6.89 –6.86 (m, 2H), 6.64 (d, *J* = 4.9 Hz, 2H), 4.21 (s, 0.14H), 3.87 (d, *J* = 3.9 Hz, 6H), 3.79 (s, 3H), 3.44 (t, *J* = 5.9 Hz, 2H), 2.90 (t, *J* = 5.8 Hz, 2H). Deuterium incorporation of **9a**: 90% D (mass).

6,7-dimethoxy-2-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinoline (10, 10a)

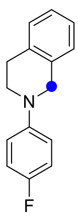


10a

10: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.68 (d, *J* = 5.1 Hz, 2H), 4.42 (s, 2H), 3.89 (d, *J* = 3.2 Hz, 6H), 3.63 (t, *J* = 5.8 Hz, 2H), 2.91 (t, *J* = 5.7 Hz, 2H).

10a: **Reaction condition: DC**: 3.5 V; 15 h, 23 mg, 27% yield, 65 D%. The crude product was purified using flash silica-gel column chromatography to afford **10a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.68 (d, *J* = 3.0 Hz, 2H), 4.41 (d, *J* = 9.8 Hz, 0.68H), 3.89 (d, *J* = 2.2 Hz, 6H), 3.63 (t, *J* = 5.8 Hz, 2H), 2.91 (t, *J* = 5.8 Hz, 2H). **^{19}F NMR** (471 MHz, $CDCl_3$) δ -61.11. Deuterium incorporation of **10a**: 60% D (mass).

2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (11, 11a)

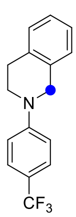


11a

11: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 – 7.14 (m, 4H), 7.03 – 6.95 (m, 4H), 4.35 (s, 2H), 3.51 (t, *J* = 5.9 Hz, 2H), 3.01 (t, *J* = 5.8 Hz, 2H).

11a: **DC**: 3.3 V; 24 h, 23 mg, 40% yield, 82 D%. The crude product was purified using flash silica-gel column chromatography to afford **11a** as white solid **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 – 7.14 (m, 4H), 7.02 – 6.95 (m, 4H), 4.34 (d, *J* = 10.1 Hz, 0.36H), 3.51 (t, *J* = 5.9 Hz, 2H), 3.00 (t, *J* = 5.8 Hz, 2H). **^{19}F NMR** (471 MHz, $CDCl_3$) δ -125.70. Deuterium incorporation of **11a**: 80% D (mass).

2-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinoline (12, 12a)

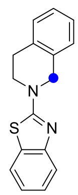


12a

12: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.8 Hz, 2H), 7.24 – 7.18 (m, 4H), 6.96 (d, *J* = 8.7 Hz, 2H), 4.50 (s, 2H), 3.65 (t, *J* = 5.9 Hz, 2H), 3.01 (t, *J* = 5.8 Hz, 2H).

12a: **Reaction condition: DC**: 3.5 V; 15 h,7 mg, 10% yield, 70 D%. The crude product was purified using flash silica-gel column chromatography to afford **12a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.8 Hz, 2H), 7.24 – 7.18 (m, 4H), 6.95 (d, J = 8.6 Hz, 2H), 4.48 (d, J = 9.8 Hz, 0.63H), 3.64 (t, J = 6.1 Hz, 2H), 3.01 (t, J = 5.9 Hz, 2H). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -61.12 (s). Deuterium incorporation of **12a**: 80% D (mass).

2-(3,4-dihydroisoquinolin-2(1H)-yl)benzo[d]thiazole (13,13a)

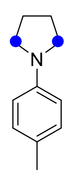


13a

13: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (t, *J* = 8 Hz, 2H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.25 – 7.20 (m, 4H), 7.09 (t, *J* = 7.6 Hz, 1H), 4.84 (s, 2H), 3.90 (t, *J* = 5.9 Hz, 2H), 3.05 (t, *J* = 5.8 Hz, 2H).

13a: **DC**: 3.9 V; 12 h,13 mg, 20% yield, 35 D%. The crude product was purified using flash silica-gel column chromatography to afford **6a** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.8, 5.0 Hz, 2H), 7.32 (t, *J* = 8.3 Hz, 1H), 7.26 – 7.18 (m, 4H), 7.10 (t, *J* = 8.1 Hz, 1H), 4.83 (d, *J* = 10.5 Hz, 1.37H), 3.90 (t, *J* = 5.9 Hz, 2H), 3.05 (t, *J* = 5.9 Hz, 2H). Deuterium incorporation of **13a**: 29% (mass).

1-(p-tolyl)pyrrolidine (14, 14a)

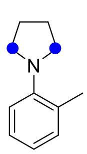


14a

14: **^{1}H NMR** (600 MHz, CDCl3) δ 7.09 (d, *J* = 8.1 Hz, 2H), 6.56 (d, *J* = 8.5 Hz, 2H), 3.33 – 3.28 (m, 4H), 2.31 (s, 3H), 2.06 – 2.02 (m, 4H).

14a: Reaction condition: **AC**: 0.5 Hz, 3.3 V (peak amplitude); 48 h, 14 mg, 34% yield, 77% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **14a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 7.08 – 7.03 (m, 2H), 6.52 (d, *J* = 8.0 Hz, 2H), 3.25 (q, *J* = 6.6 Hz, 0.92H), 2.27 (s, 3H), 1.99 (d, *J* = 4.2 Hz, 4H). Deuterium incorporation of **14a**: 50% (mass).

1-(o-tolyl)pyrrolidine (15, 15a)

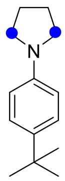


15a

15: **^{1}H NMR** (600 MHz, CDCl3) δ 7.13 (t, *J* = 7.0 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 3.21 (d, *J* = 6.3 Hz, 4H), 2.35 (s, 3H), 1.95 (qd, *J* = 7.1, 4.6, 3.1 Hz, 4H).

15a: Reaction condition: **AC**: 0.5 Hz, 3.1 V (peak amplitude); 48 h, 16 mg, 38% yield, 36% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **15a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 7.14 (t, *J* = 7.0 Hz, 2H), 6.93 – 6.90 (m, 1H), 6.86 (t, *J* = 7.3 Hz, 1H), 3.24 – 3.17 (m, 2.51H), 2.36 (s, 3H), 1.97 – 1.94 (m, 4H). Deuterium incorporation of **15a**: 36% (mass).

1-(4-(tert-butyl)phenyl)pyrrolidine (16, 16a)

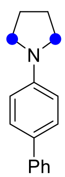


16a

16: **^{1}H NMR** (600 MHz, CDCl3) δ 7.31 (d, *J* = 8.8 Hz, 2H), 6.58 (d, *J* = 8.7 Hz, 2H), 3.33 – 3.29 (m, 4H), 2.04 – 2.00 (m, 4H), 1.34 (s, 9H).

16a: Reaction condition: **AC**: 0.5 Hz, 3.3 V (peak amplitude); 48 h, 20mg, 38% yield, 75% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **16a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 7.27 – 7.24 (m, 2H), 6.53 (d, *J* = 8.2 Hz, 2H), 3.25 (q, *J* = 6.4 Hz, 1.02H), 1.97 (d, *J* = 8.2 Hz, 4H), 1.29 (s, 9H). Deuterium incorporation of **16a**: 70% (mass).

1-([1,1'-biphenyl]-4-yl)pyrrolidine (17, 17a)

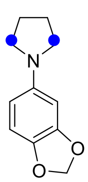


17a

17: **^{1}H NMR** (600 MHz, CDCl3) δ 7.59 (d, *J* = 7.8 Hz, 2H), 7.54 (d, *J* = 8.9 Hz, 2H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 14.7 Hz, 1H), 6.67 (d, *J* = 8.8 Hz, 2H), 3.40 – 3.32 (m, 4H), 2.09 – 2.01 (m, 4H).

17a: Reaction condition: **AC**: 0.5 Hz, 3.3 V (peak amplitude); 48 h, 13 mg, 23% yield, 52% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **17a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 7.60 – 7.55 (m, 2H), 7.55 – 7.50 (m, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.28 – 7.24 (m, 1H), 6.66 (d, *J* = 8.1 Hz, 2H), 3.39 – 3.31 (m, 1.91H), 2.08 – 1.98 (m, 4H). Deuterium incorporation of **17a**: 46% (mass).

1-(benzo[d][1,3]dioxol-5-yl)pyrrolidine (18, 18a)

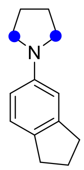


18a

18: **^{1}H NMR** (600 MHz, CDCl3) δ 6.74 (d, *J* = 8.4 Hz, 1H), 6.24 (d, *J* = 2.4 Hz, 1H), 5.98 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.86 (s, 2H), 3.27 – 3.17 (m, 4H), 2.02 – 1.96 (m, 4H).

18a: Reaction condition: **AC**: 0.5 Hz, 3.1 V (peak amplitude); 48 h, 14 mg, 28% yield, 75% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **18a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 6.73 (d, *J* = 8.4 Hz, 1H), 6.24 (s, 1H), 5.98 (d, *J* = 8.4 Hz, 1H), 5.86 (s, 2H), 3.21 (q, *J* = 6.4 Hz, 0.98H), 1.99 (d, *J* = 4.1 Hz, 4H). Deuterium incorporation of **18a**: 48% (mass).

1-(2,3-dihydro-1H-inden-5-yl)pyrrolidine (19, 19a)

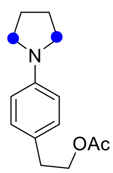


19a

19: **^{1}H NMR** (600 MHz, CDCl3) δ 7.12 (d, *J* = 8.1 Hz, 1H), 6.53 (s, 1H), 6.43 (d, *J* = 8.2 Hz, 1H), 3.33 – 3.27 (m, 4H), 2.88 (dt, *J* = 19.3, 7.3 Hz, 4H), 2.09 (q, *J* = 7.3 Hz, 2H), 2.04 – 1.99 (m, 4H).

19a: Reaction condition: **AC**: 0.5 Hz, 3.3 V (peak amplitude); 48 h, 20 mg, 42% yield, 24% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **19a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 7.10 (d, *J* = 8.1 Hz, 1H), 6.52 (s, 1H), 6.46 – 6.38 (m, 1H), 3.28 (q, *J* = 6.0 Hz, 3.05H), 2.86 (dt, *J* = 28.9, 7.3 Hz, 4H), 2.06 (p, *J* = 7.3 Hz, 2H), 2.00 (q, *J* = 5.5, 4.0 Hz, 4H). Deuterium incorporation of **19a**: 23% (mass).

4-(pyrrolidin-1-yl)phenethyl acetate (20, 20a)

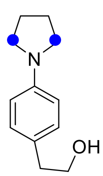


20a

20: **^{1}H NMR** (600 MHz, CDCl3) δ 7.09 (d, *J* = 8.5 Hz, 2H), 6.54 (d, *J* = 8.5 Hz, 2H), 4.24 (t, *J* = 7.2 Hz, 2H), 3.31 – 3.26 (m, 4H), 2.85 (t, *J* = 7.2 Hz, 2H), 2.06 (s, 3H), 2.03 – 1.98 (m, 4H).

20a: Reaction condition: **AC**: 0.5 Hz, 3.3 V (peak amplitude); 48 h, 21 mg, 36% yield, 89% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **20a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 7.09 (d, *J* = 8.1 Hz, 2H), 6.52 (d, *J* = 7.9 Hz, 2H), 4.23 (t, *J* = 7.3 Hz, 2H), 3.25 (s, 0.44H), 2.84 (t, *J* = 7.2 Hz, 2H), 2.05 (s, 3H), 1.99 (s, 4H). Deuterium incorporation of **20a**: 75% (mass).

2-(4-(pyrrolidin-1-yl)phenyl)ethan-1-ol (21, 21a)

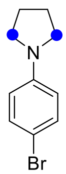


21a

21: **^{1}H NMR** (600 MHz, CDCl3) δ 7.10 (d, *J* = 8.0 Hz, 2H), 6.55 (s, 2H), 3.81 (q, *J* = 6.3 Hz, 2H), 3.27 (d, *J* = 6.3 Hz, 4H), 2.78 (t, *J* = 6.5 Hz, 2H), 2.00 (d, *J* = 6.1 Hz, 4H).

21a: Reaction condition: **AC**: 0.5 Hz, 3.3 V (peak amplitude); 48 h, 20 mg, 40% yield, 54% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **21a** as a white solid. **^{1}H NMR** (600 MHz, CDCl3) δ 7.13 – 7.06 (m, 2H), 6.55 (d, *J* = 8.1 Hz, 2H), 3.81 (t, *J* = 6.6 Hz, 2H), 3.28 (dd, *J* = 12.4, 6.2 Hz, 1.82H), 2.78 (t, *J* = 6.6 Hz, 2H), 2.03 – 1.97 (m, 4H). Deuterium incorporation of **21a**: 41% (mass).

1-(4-bromophenyl)pyrrolidine (22, 22a)

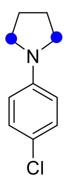


22a

22: ^{1}**H NMR** (600 MHz, CDCl3) δ 7.29 (d, *J* = 8.9 Hz, 2H), 6.43 (d, *J* = 8.9 Hz, 2H), 3.28 – 3.22 (m, 4H), 2.05 – 1.97 (m, 4H).

22a: Reaction condition: **AC**: 0.5 Hz, 3.5 V (peak amplitude); 48 h, 23 mg, 40% yield, 23% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **22a** as a white solid. ^{1}**H NMR** (600 MHz, CDCl3) δ 7.30 – 7.27 (m, 2H), 6.44 (d, *J* = 8.5 Hz, 2H), 3.25 (td, *J* = 8.0, 7.3, 4.2 Hz, 3.1H), 2.04 – 1.99 (m, 4H). Deuterium incorporation of **22a**: 41% (mass).

1-(4-chlorophenyl)pyrrolidine (23, 23a)

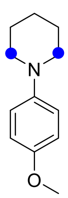


23a

23: ^{1}**H NMR** (600 MHz, CDCl3) δ 7.17 (d, *J* = 8.9 Hz, 2H), 6.48 (d, *J* = 8.9 Hz, 2H), 3.28 – 3.24 (m, 4H), 2.05 – 2.00 (m, 4H).

23a: Reaction condition: **AC**: 0.5 Hz, 3.4 V (peak amplitude); 48 h, 19 mg, 42% yield, 36% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **23a** as a white solid. ^{1}**H NMR** (600 MHz, CDCl3) δ 7.19 – 7.13 (m, 2H), 6.48 (d, *J* = 8.5 Hz, 2H), 3.28 – 3.21 (m, 2.54H), 2.03 – 1.99 (m, 4H). Deuterium incorporation of **23a**: 32% (mass).

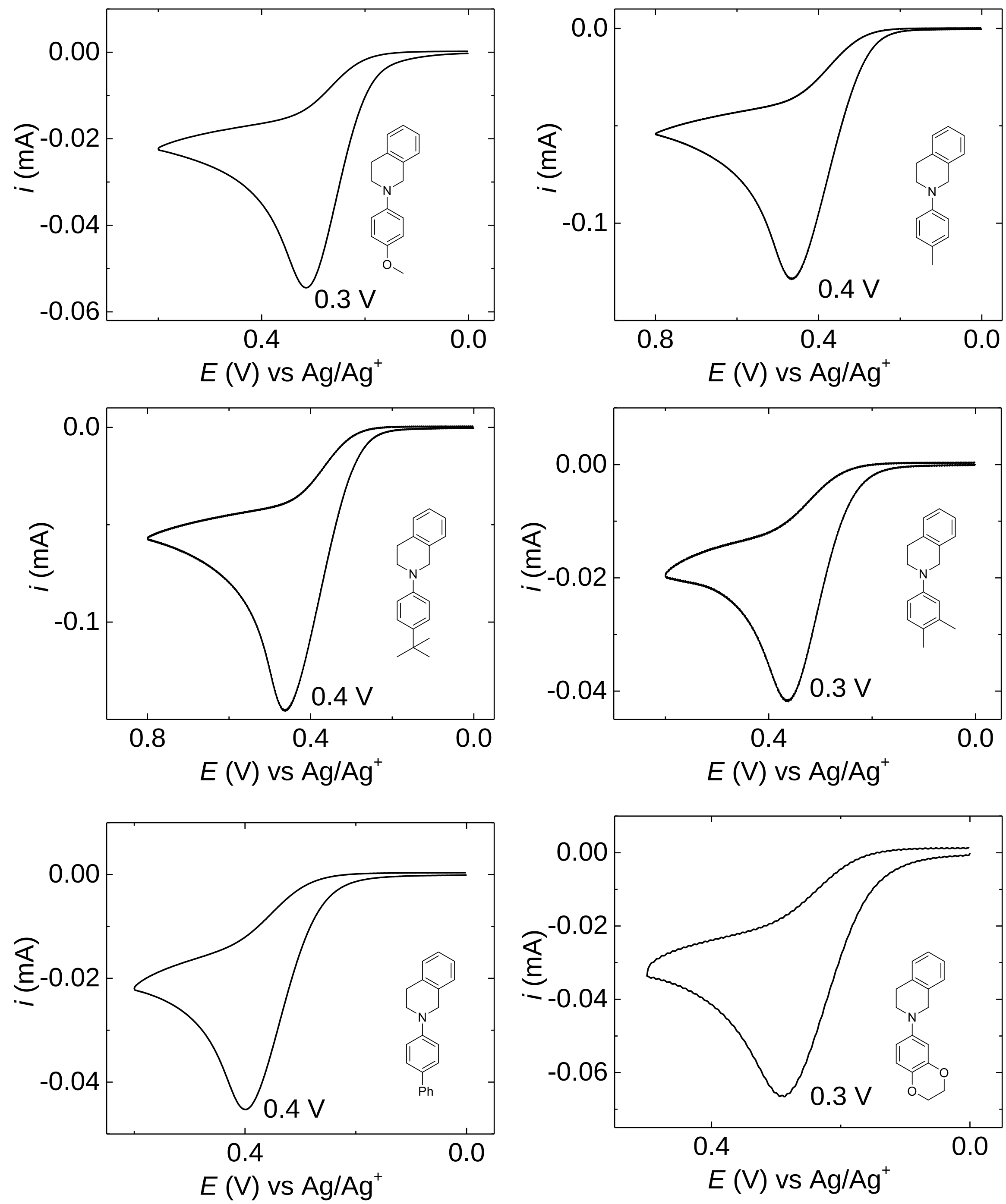
1-(4-methoxyphenyl)piperidine (24, 24a)

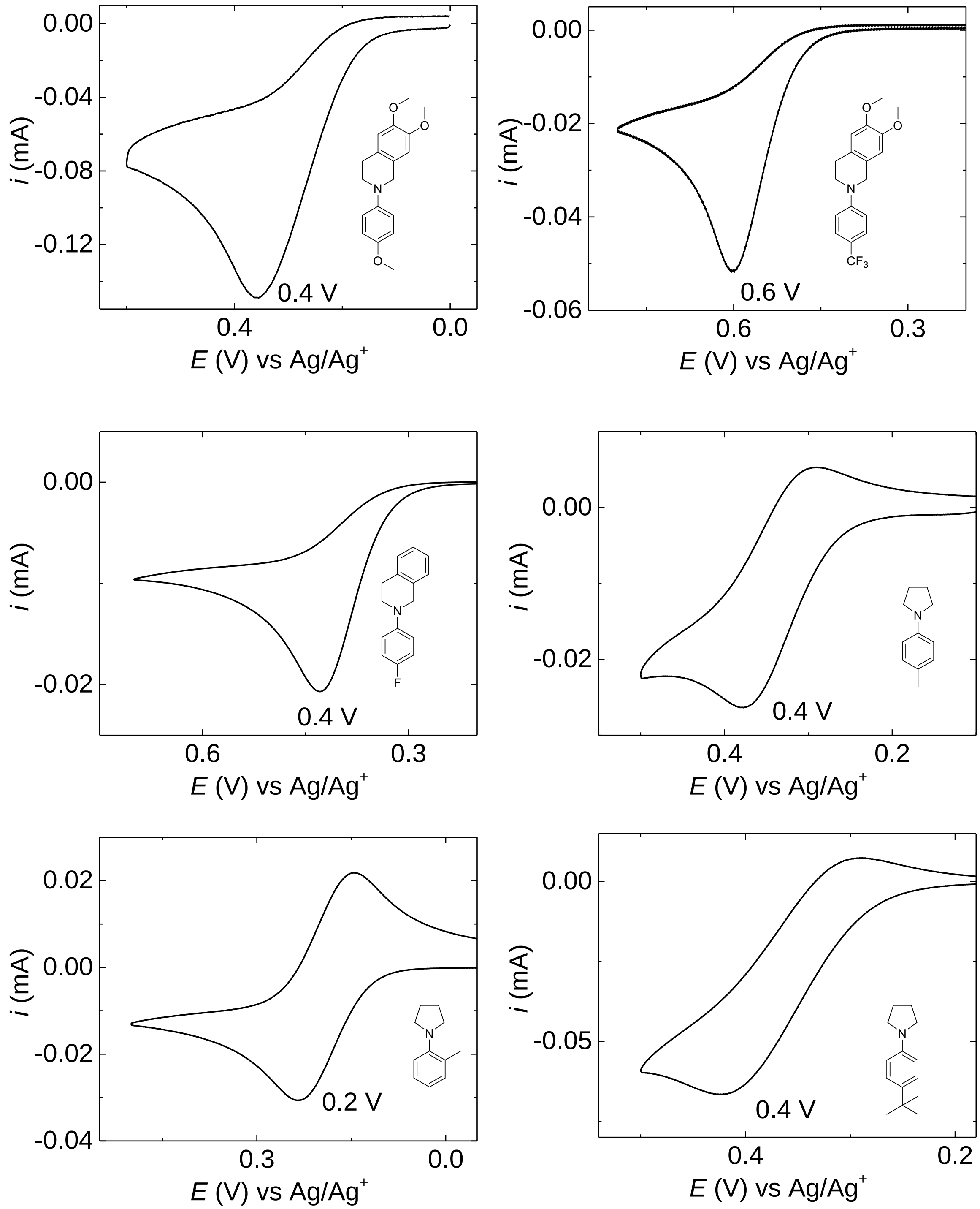


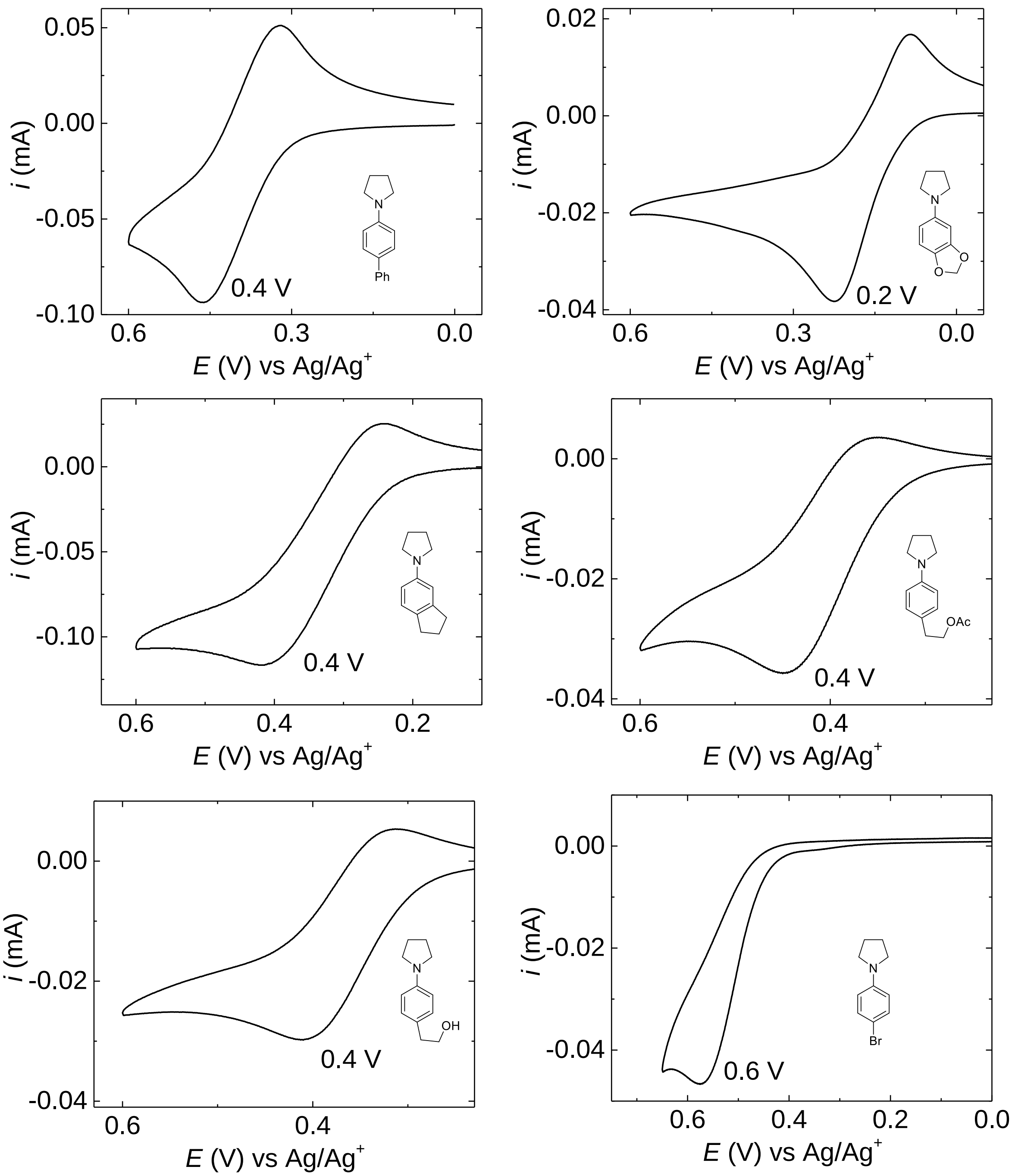
24: ^{1}**H NMR** (600 MHz, CDCl3) δ 6.93 (d, *J* = 9.0 Hz, 2H), 6.86 – 6.81 (m, 2H), 3.78 (s, 3H), 3.06 – 3.01 (m, 4H), 1.74 (p, *J* = 5.8 Hz, 4H), 1.56 (q, *J* = 6.1 Hz, 2H).

24a: Reaction condition: **AC**: 50 Hz, 3.4 V (peak amplitude); 48 h, 25 mg, 51% yield, 50% D. The crude product was purified using flash silica-gel column chromatography (Ethyl acetate: Hexane = 10:90 v/v) to afford **24a** as a white solid. ^{1}**H NMR** (600 MHz, CDCl3) δ 6.93 (d, *J* = 8.7 Hz, 2H), 6.87 – 6.81 (m, 2H), 3.78 (s, 3H), 3.02 (dt, *J* = 16.9, 5.4 Hz, 1.99H), 1.73 (q, *J* = 5.8 Hz, 4H), 1.56 (tdd, *J* = 9.5, 5.9, 3.9 Hz, 2H). Deuterium incorporation of **24a**: 45% (mass).

10. Oxidation potentials of tetrahydroisoquinolines **(3-13),** pyrrolidine **(14-23),** and piperidines **(24)**




i (mA)
E (V) vs Ag/Ag+
0.00
-0.04
-0.08
-0.12
0.4
0.0
0.4 V
0.00
-0.02
-0.04
-0.06
0.6
0.3
0.6 V
CF3
F
0.4 V
0.6
0.3
-0.02
0.00
0.4 V
0.4
0.2
0.02
0.00
-0.02
-0.04
0.3
0.0
0.2 V
0.00
-0.05
0.4
0.2
0.4 V



0.05
0.00
-0.05
-0.10
i (mA)
0.6
0.3
0.0
E (V) vs Ag/Ag+
0.4 V
N
Ph
0.02
0.00
-0.02
-0.04
i (mA)
0.6
0.3
0.0
E (V) vs Ag/Ag+
0.2 V
N
O
O
0.00
-0.05
-0.10
i (mA)
0.6
0.4
0.2
E (V) vs Ag/Ag+
0.4 V
N
0.00
-0.02
-0.04
i (mA)
0.6
0.4
E (V) vs Ag/Ag+
0.4 V
N
OAc
0.00
-0.02
-0.04
i (mA)
0.6
0.4
E (V) vs Ag/Ag+
0.4 V
N
OH
0.00
-0.02
-0.04
i (mA)
0.6
0.4
0.2
0.0
E (V) vs Ag/Ag+
0.6 V
N
Br

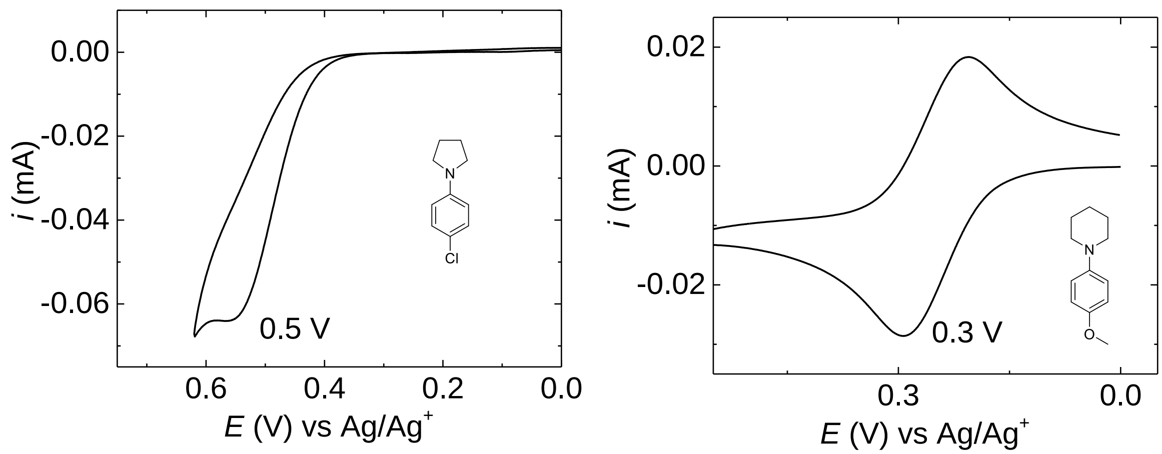
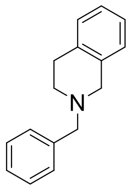


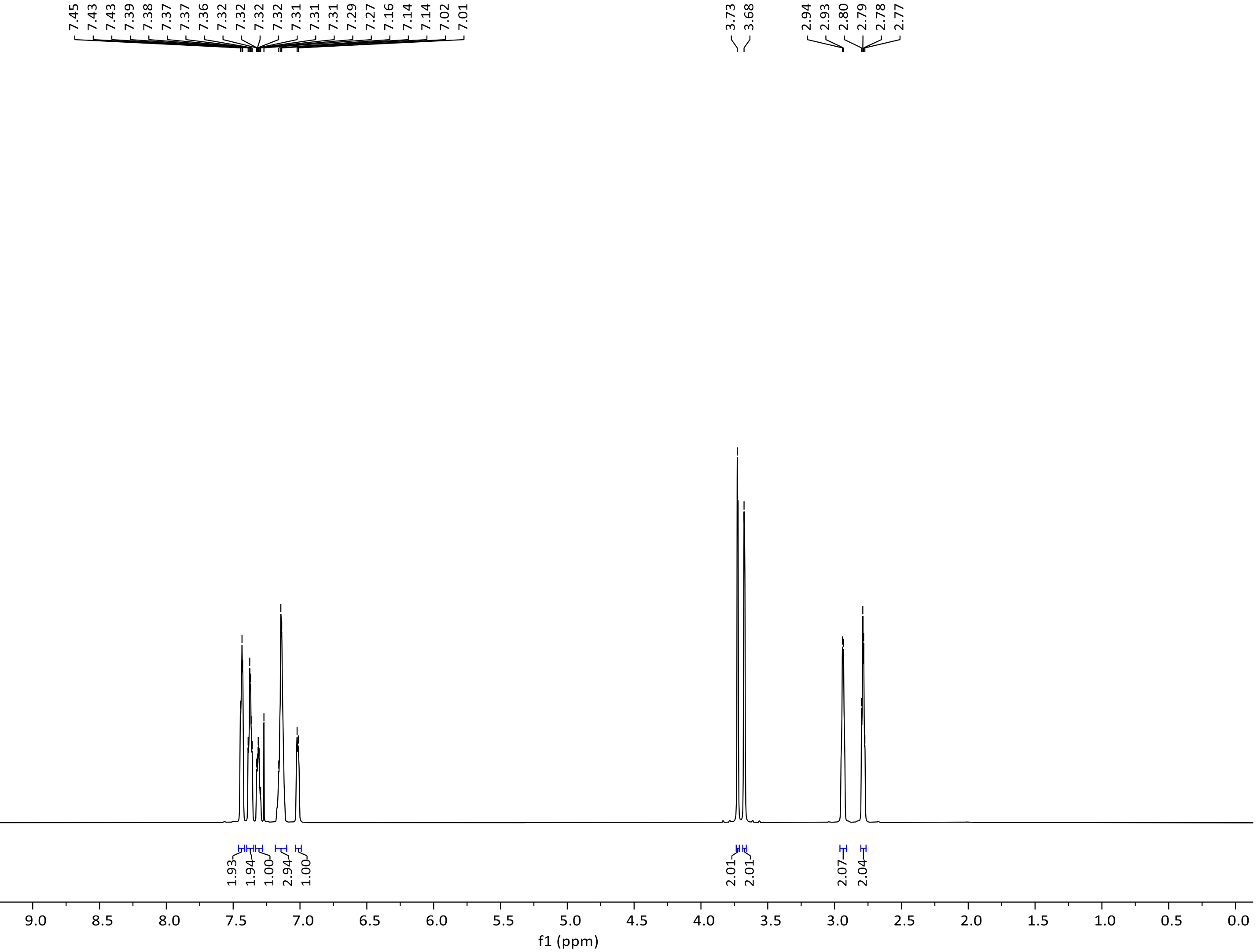
Fig. S5. Cyclic voltammograms of **3-24** in anhydrous DMA containing 0.1 M $LiClO_4$. Scan rate 0.1 V/s.

11. References

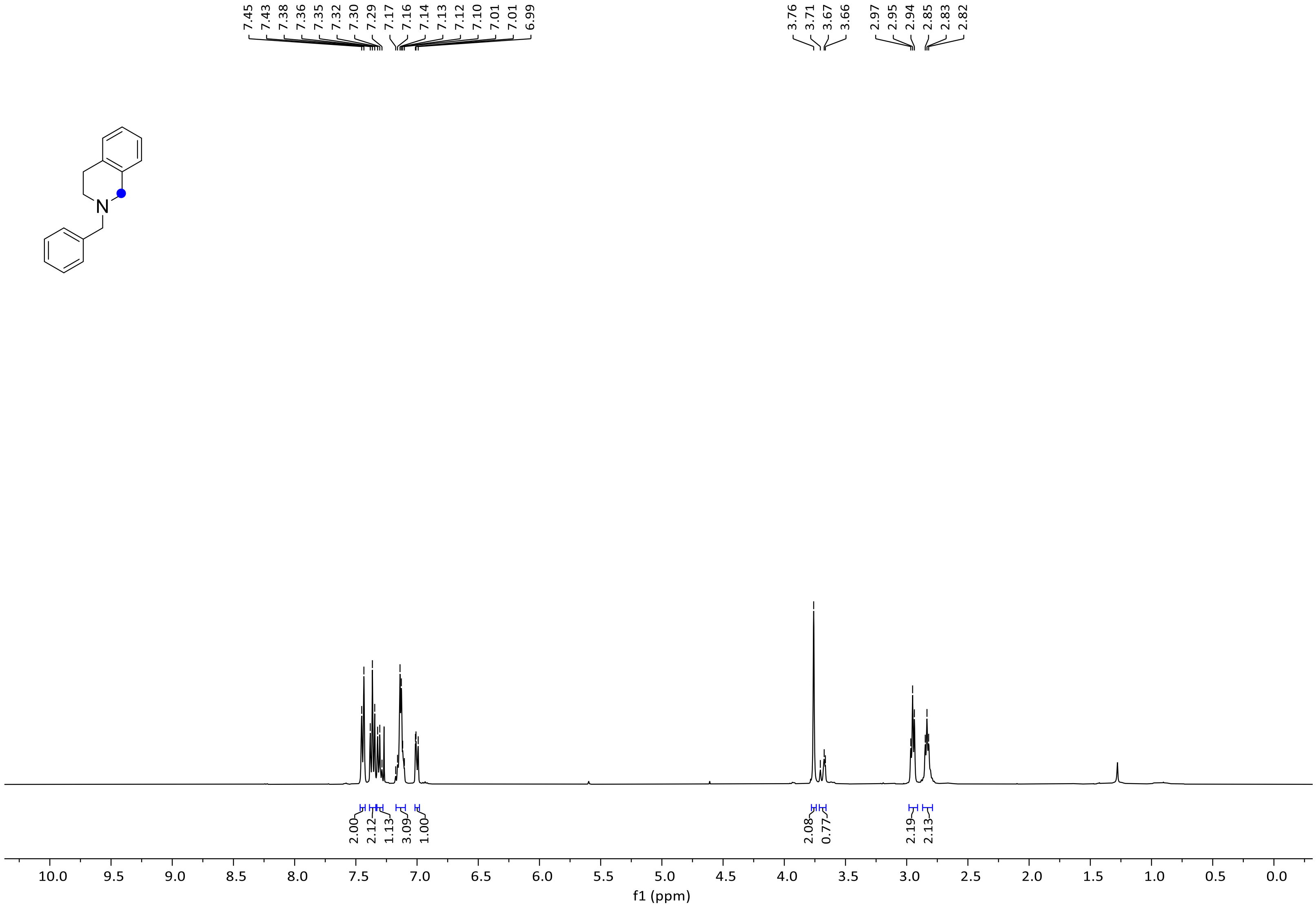
1. Matsumoto, K.; Takeda, S.; Hirokane, T.; Yoshida, M., A Highly Selective Palladium-Catalyzed Aerobic Oxidative Aniline–Aniline Cross-Coupling Reaction. *Organic Letters* **2019,** *21* (18), 7279-7283.
2. Zhang, Z.; Miao, C.; Xia, C.; Sun, W., Synergistic acid-catalyzed synthesis of N-aryl-substituted azacycles from anilines and cyclic ethers. *Org. Lett.* **2016,** *18* (7), 1522-1525.
3. Fang, Z.; Ning, Y.; Mi, P.; Liao, P.; Bi, X., Catalytic C–H α-Trifluoromethylation of α,β-Unsaturated Carbonyl Compounds. *Organic Letters* **2014,** *16* (5), 1522-1525.
4. Wu, J.; Tongdee, S.; Ammaiyappan, Y.; Darcel, C., A Concise Route to Cyclic Amines from Nitroarenes and Ketoacids under Iron-Catalyzed Hydrosilylation Conditions. *Advanced Synthesis & Catalysis* **2021,** *363* (15), 3859-3865.
5. Hatakeyama, T.; Yoshimoto, Y.; Ghorai, S. K.; Nakamura, M., Transition-Metal-Free Electrophilic Amination between Aryl Grignard Reagents and N-Chloroamines. *Organic Letters* **2010,** *12* (7), 1516-1519.
6. Feng, T.; Wang, S.; Liu, Y.; Liu, S.; Qiu, Y., Electrochemical Desaturative β-Acylation of Cyclic N-Aryl Amines. *Angewandte Chemie International Edition* **2022,** *61* (6), e202115178.
7. Mudithanapelli, C.; Dhorma, L. P.; Kim, M.-h., PIFA-Promoted, Solvent-Controlled Selective Functionalization of C(sp2)–H or C(sp3)–H: Nitration via C–N Bond Cleavage of CH3NO2, Cyanation, or Oxygenation in Water. *Organic Letters* **2019,** *21* (9), 3098-3102.
8. Xia, Q.; Li, Y.; Wang, X.; Dai, P.; Deng, H.; Zhang, W.-H., Visible Light-Driven α-Alkylation of N-Aryl tetrahydroisoquinolines Initiated by Electron Donor–Acceptor Complexes. *Organic Letters* **2020,** *22* (18), 7290-7294.
9. Zhang, G.; Ma, Y.; Cheng, G.; Liu, D.; Wang, R., A Unique Combined Source of “CN” from 1,2-Dichloroethane and TMSN3 in the Copper-Catalyzed Cyanation of a C(sp3)–H Bond Adjacent to a Nitrogen Atom. *Organic Letters* **2014,** *16* (3), 656-659.
10. Jones, K. M.; Karier, P.; Klussmann, M., C1-Substituted N-Alkyl Tetrahydroisoquinoline Derivatives through V-Catalyzed Oxidative Coupling. *ChemCatChem* **2012,** *4* (1), 51-54.
11. Rodrigo, S.; Um, C.; Mixdorf, J. C.; Gunasekera, D.; Nguyen, H. M.; Luo, L., Alternating Current Electrolysis for Organic Electrosynthesis: Trifluoromethylation of (Hetero)arenes. *Org. Lett.* **2020,** *22* (17), 6719-6723.
12. Gunasekera, D.; Mahajan, J. P.; Wanzi, Y.; Rodrigo, S.; Liu, W.; Tan, T.; Luo, L., Controlling One- or Two-Electron Oxidation for Selective Amine Functionalization by Alternating Current Frequency. *J. Am. Chem. Soc.* **2022,** *144* (22), 9874-9882.
13. Mayer, J. M., Understanding Hydrogen Atom Transfer: From Bond Strengths to Marcus Theory. *Acc. Chem. Res.* **2011,** *44* (1), 36-46.
14. Bard, A. J.; Faulkner, L. R., *Electrochemical methods: fundamentals and applications*. Wiley New York: 1980.
15. Gruber, C. C.; Oberdorfer, G.; Voss, C. V.; Kremsner, J. M.; Kappe, C. O.; Kroutil, W., An algorithm for the deconvolution of mass spectrosopic patterns in isotope labeling studies. evaluation for the hydrogen− deuterium exchange reaction in ketones. *The Journal of organic chemistry* **2007,** *72* (15), 5778-5783.

Appendix A. Copies of ^1H and ^{19}F NMR spectra

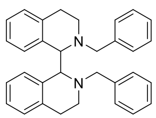


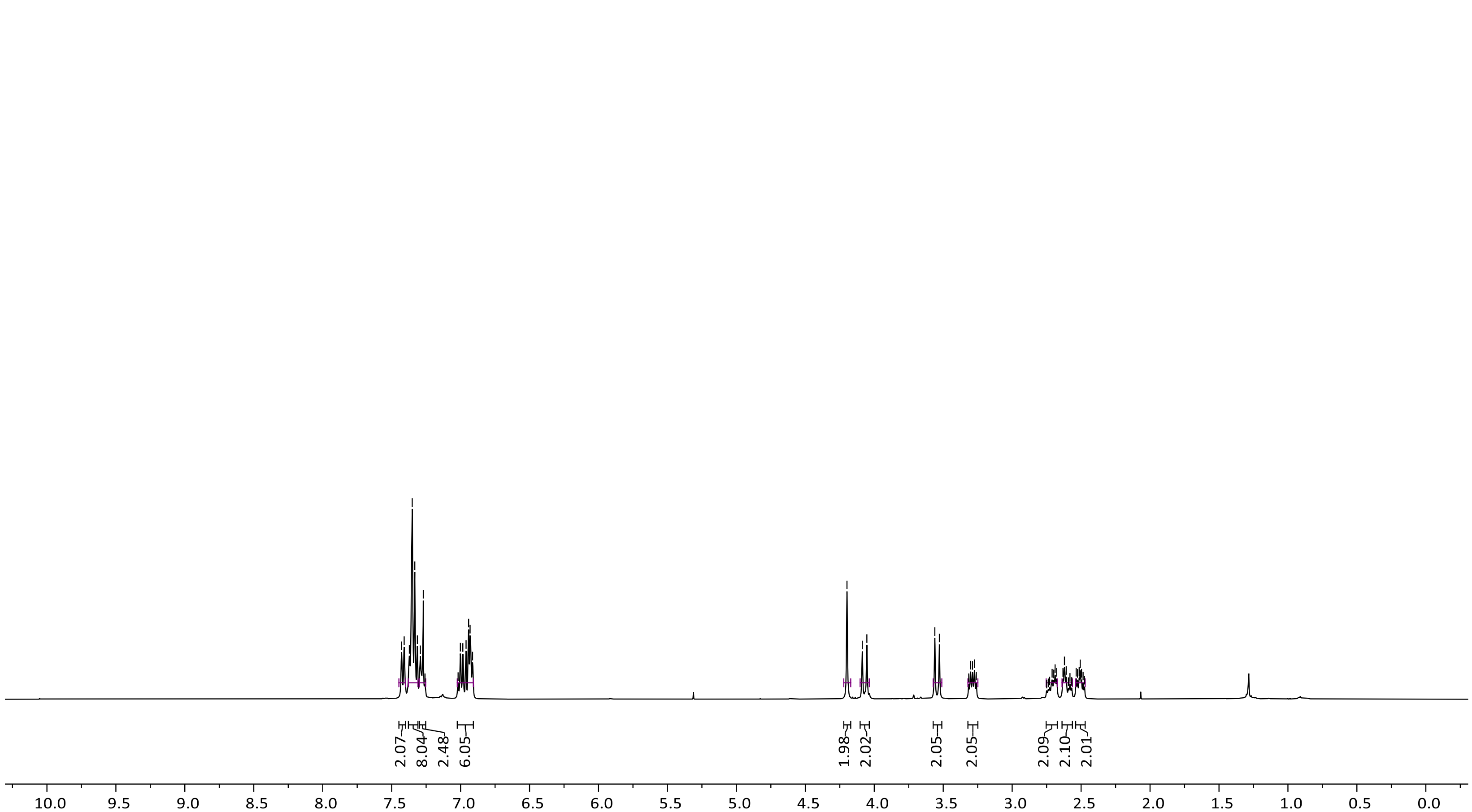


^1H NMR spectrum of **01** (600 MHz, $CDCl_3$)

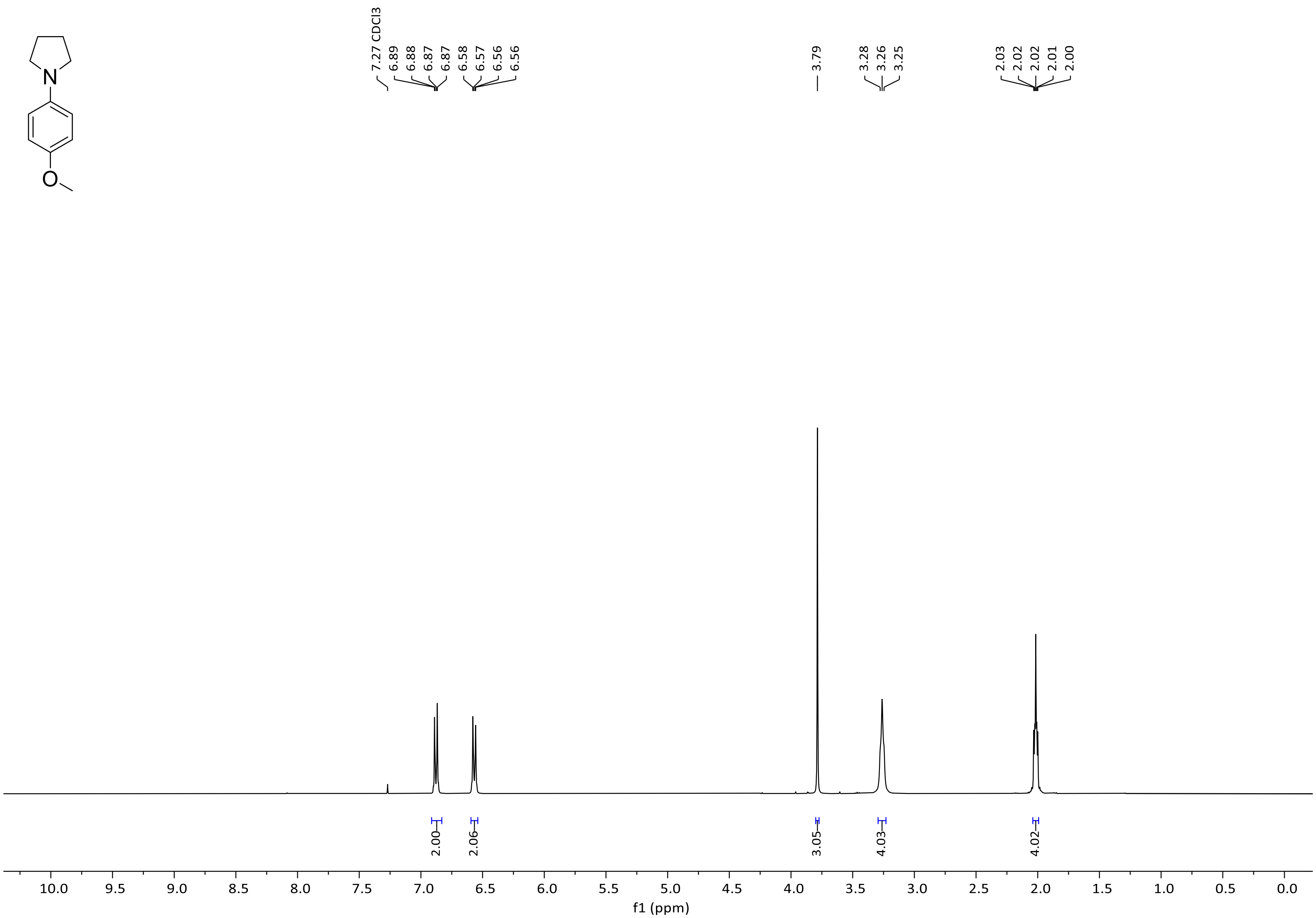


^{1}H NMR spectrum of **1a** (600 MHz, $CDCl_3$)

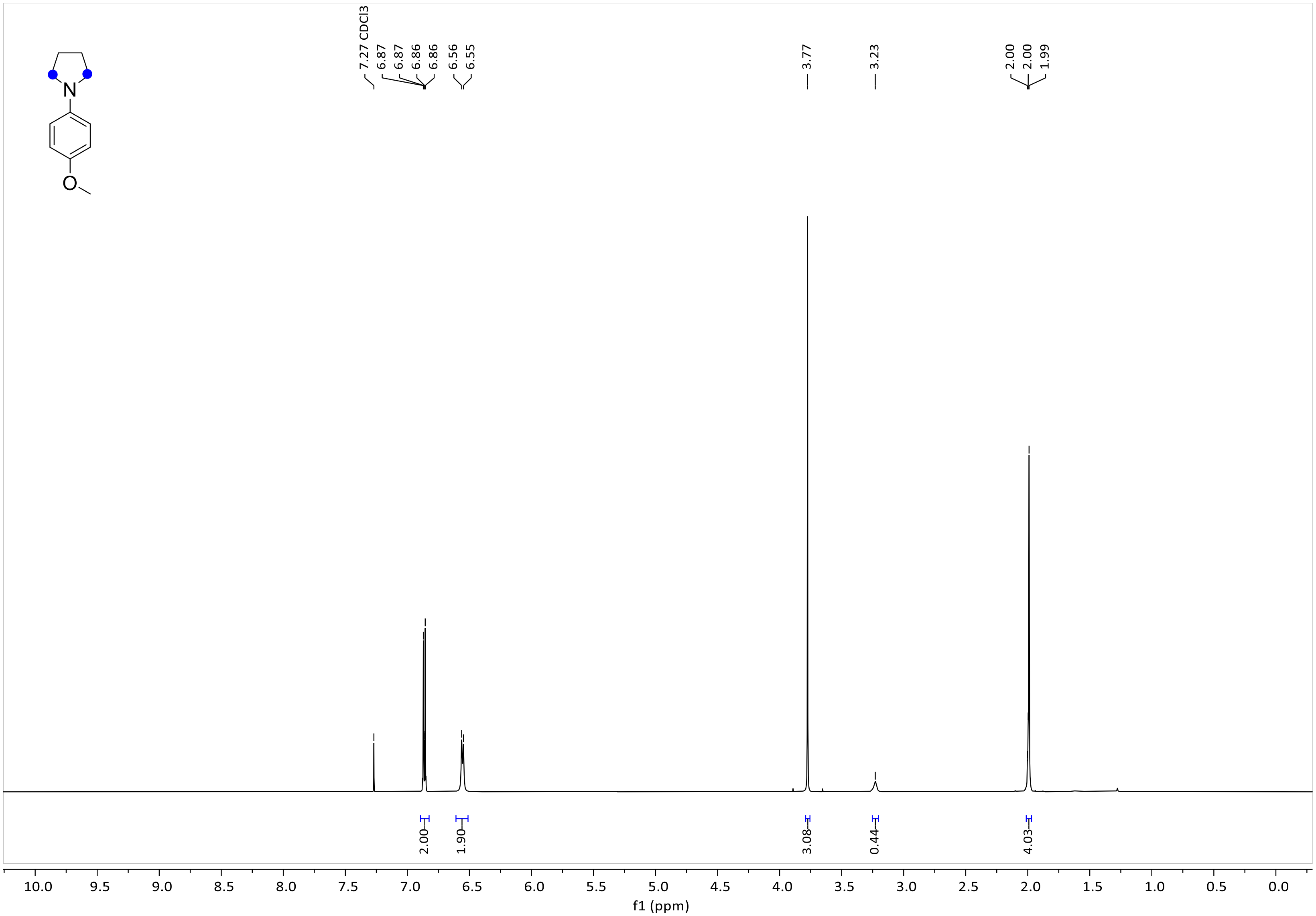




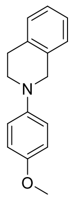
[1]H NMR spectrum of dimer (600 MHz, $CDCl_3$)

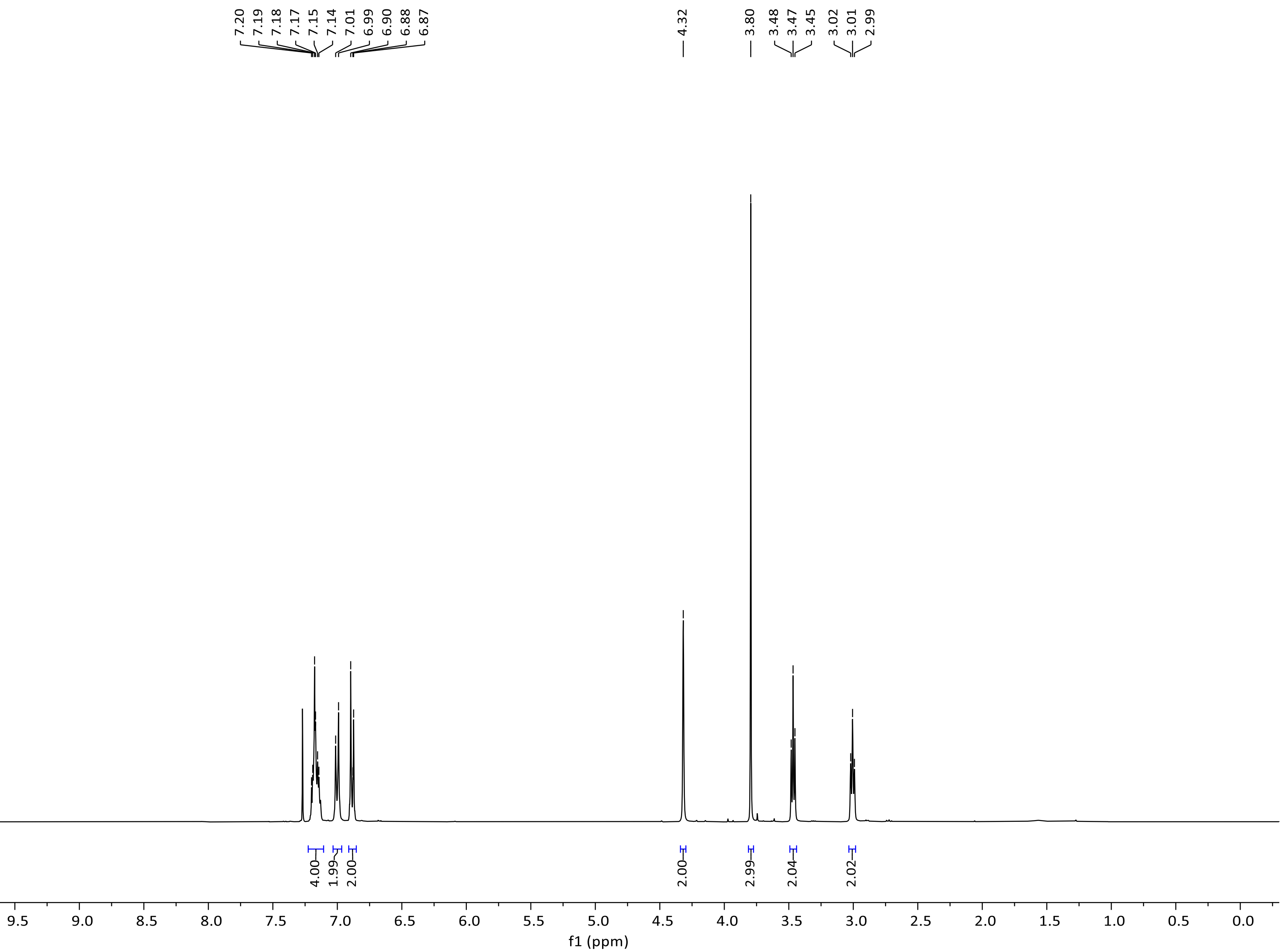


^{1}H NMR spectrum of **02** (600 MHz, $CDCl_3$)

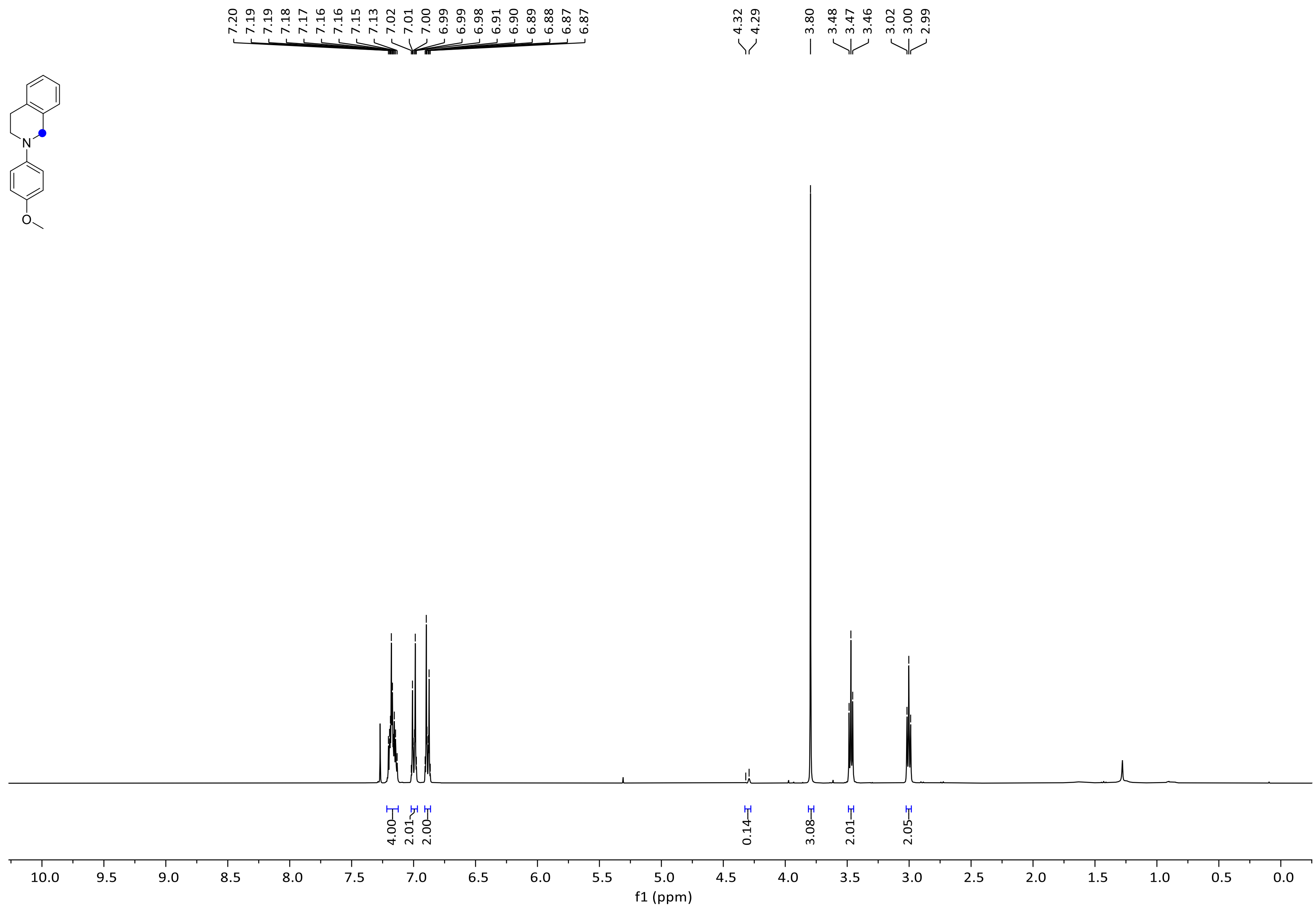


^{1}H NMR spectrum of **2a** (600 MHz, $CDCl_3$)

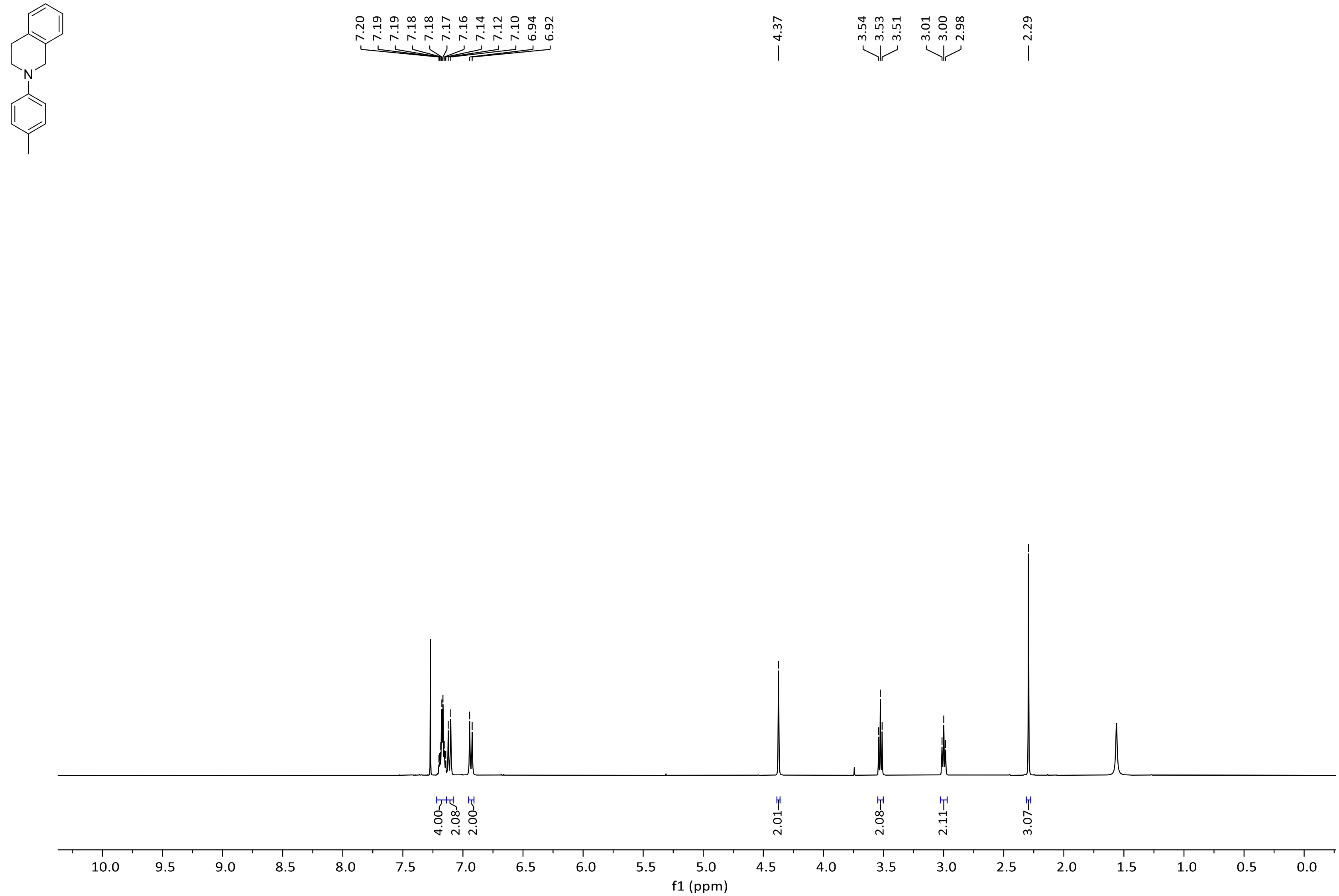




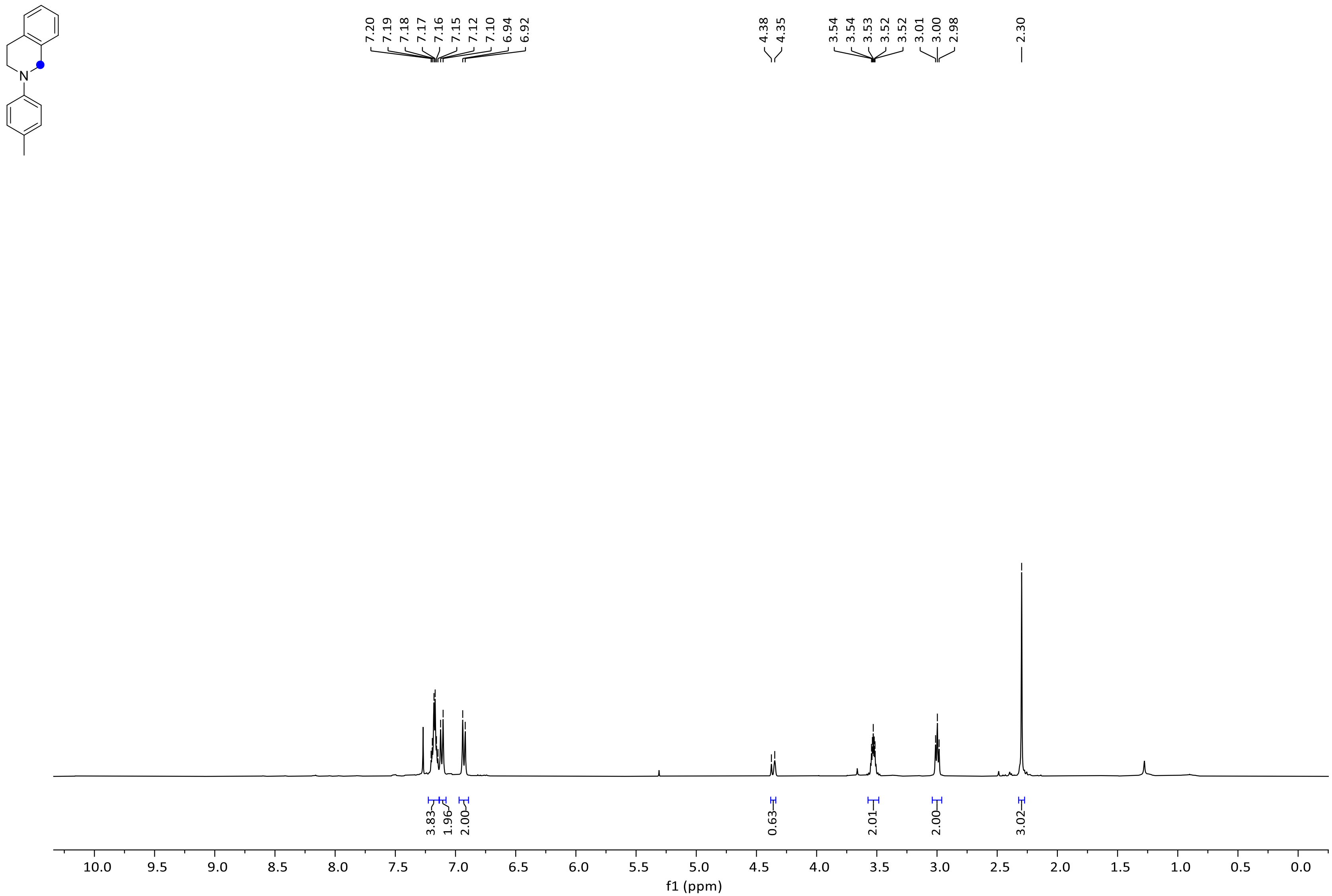
^{1}H NMR spectrum of **03** (600 MHz, $CDCl_3$)



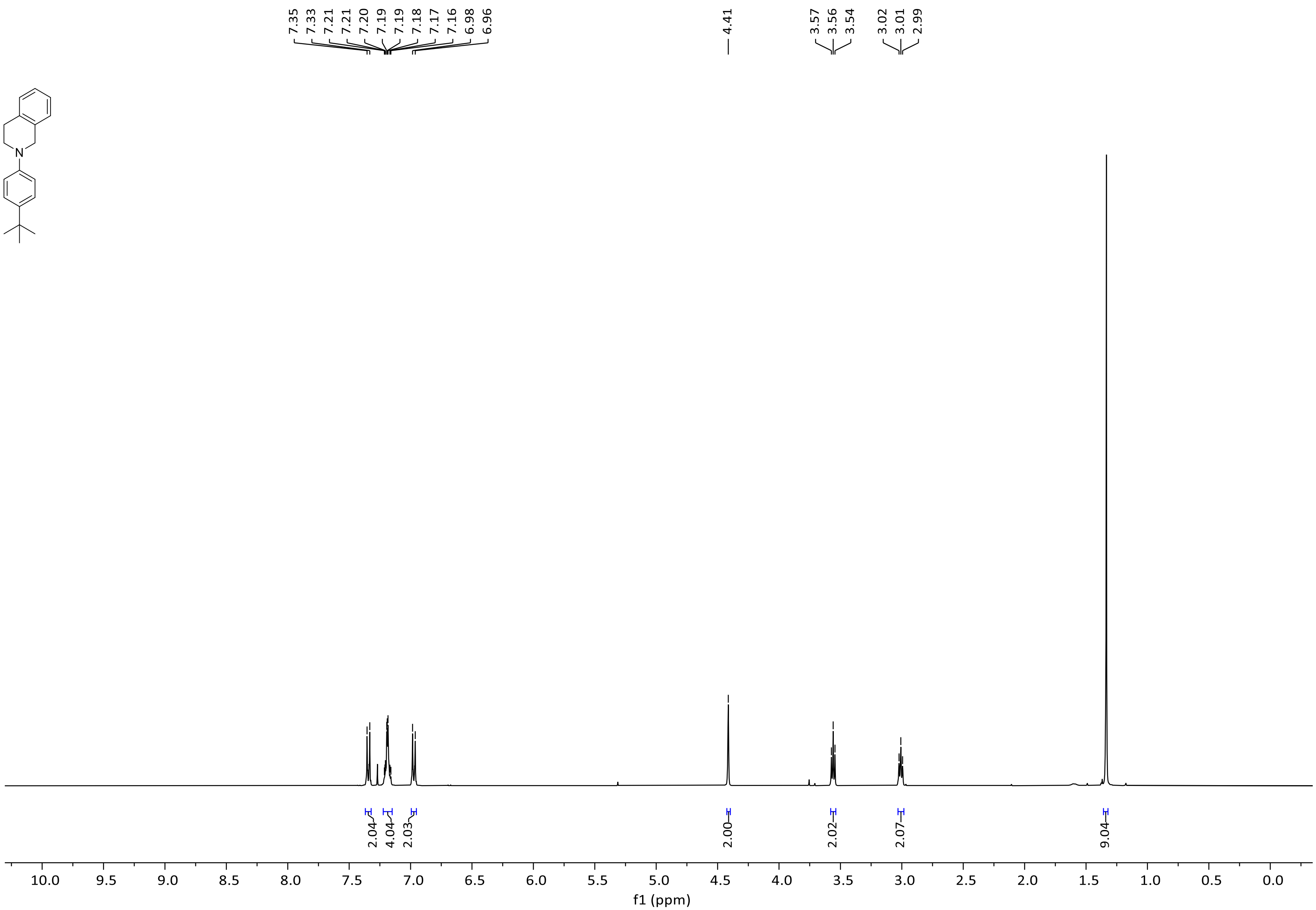
^{1}H NMR spectrum of **3a** (600 MHz, $CDCl_3$)



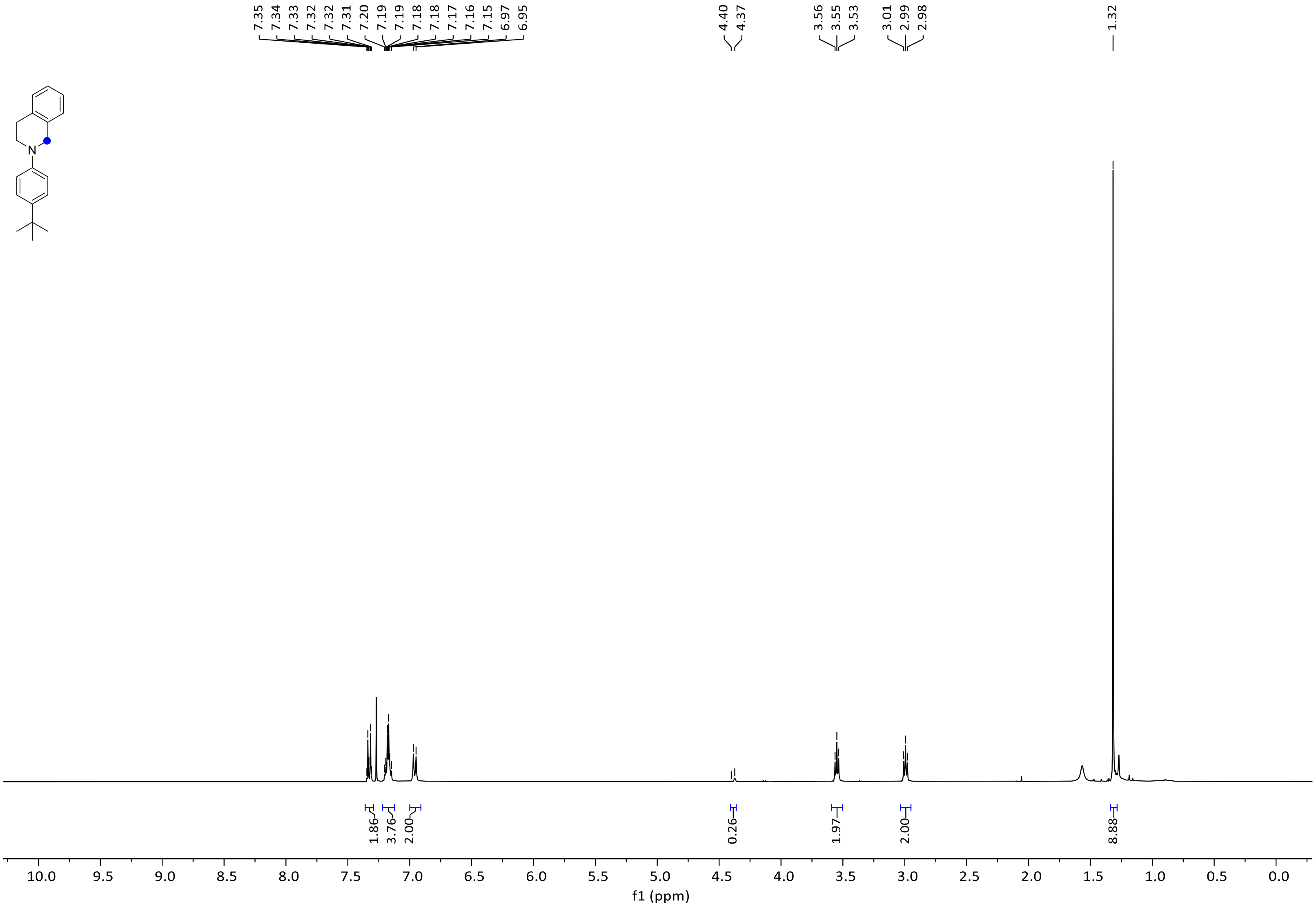
^{1}H NMR spectrum of **04** (600 MHz, $CDCl_3$)



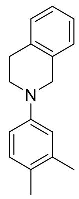
[1]H NMR spectrum of **4a** (600 MHz, $CDCl_3$)

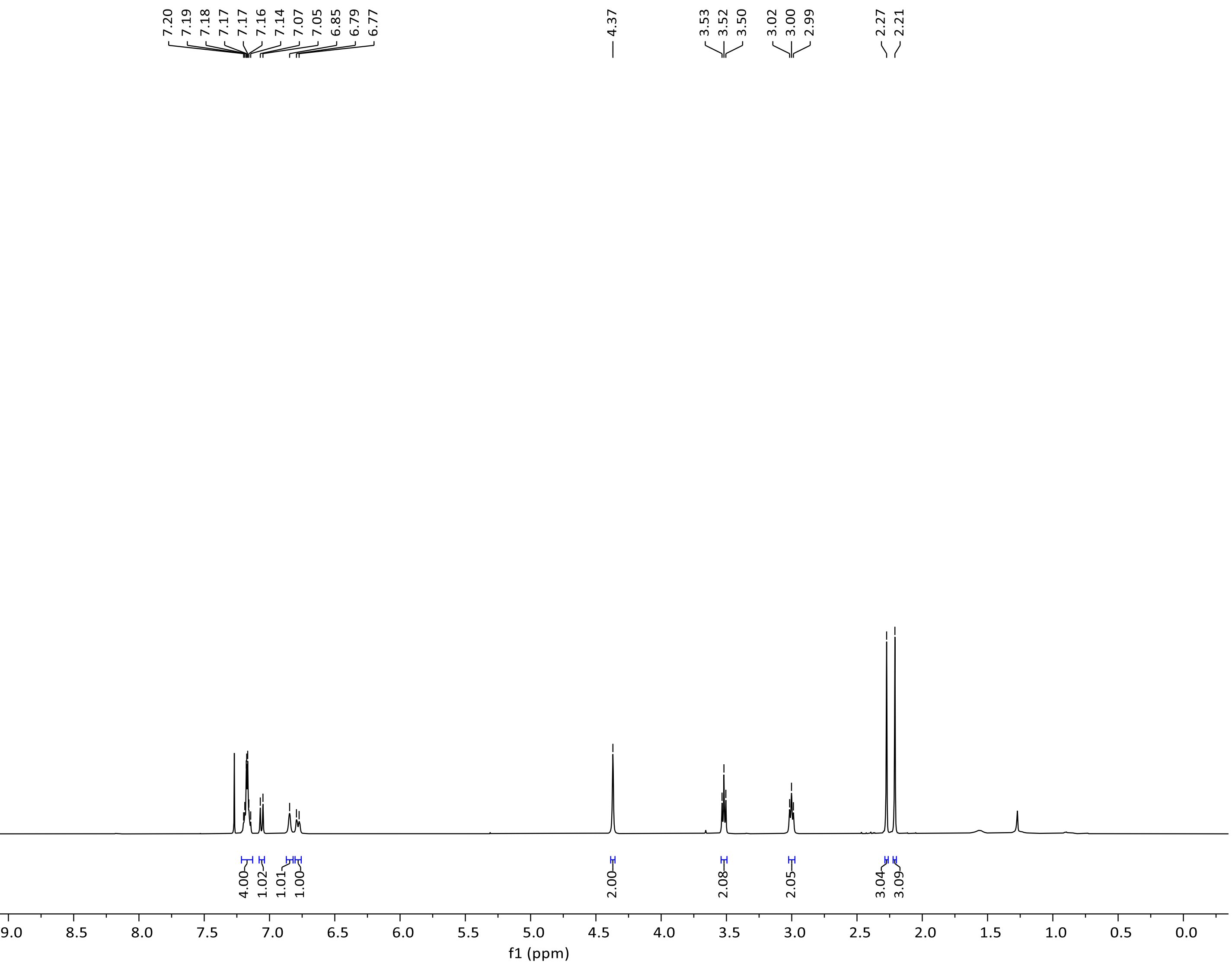


^{1}H NMR spectrum of **05** (600 MHz, $CDCl_3$)

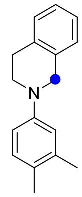


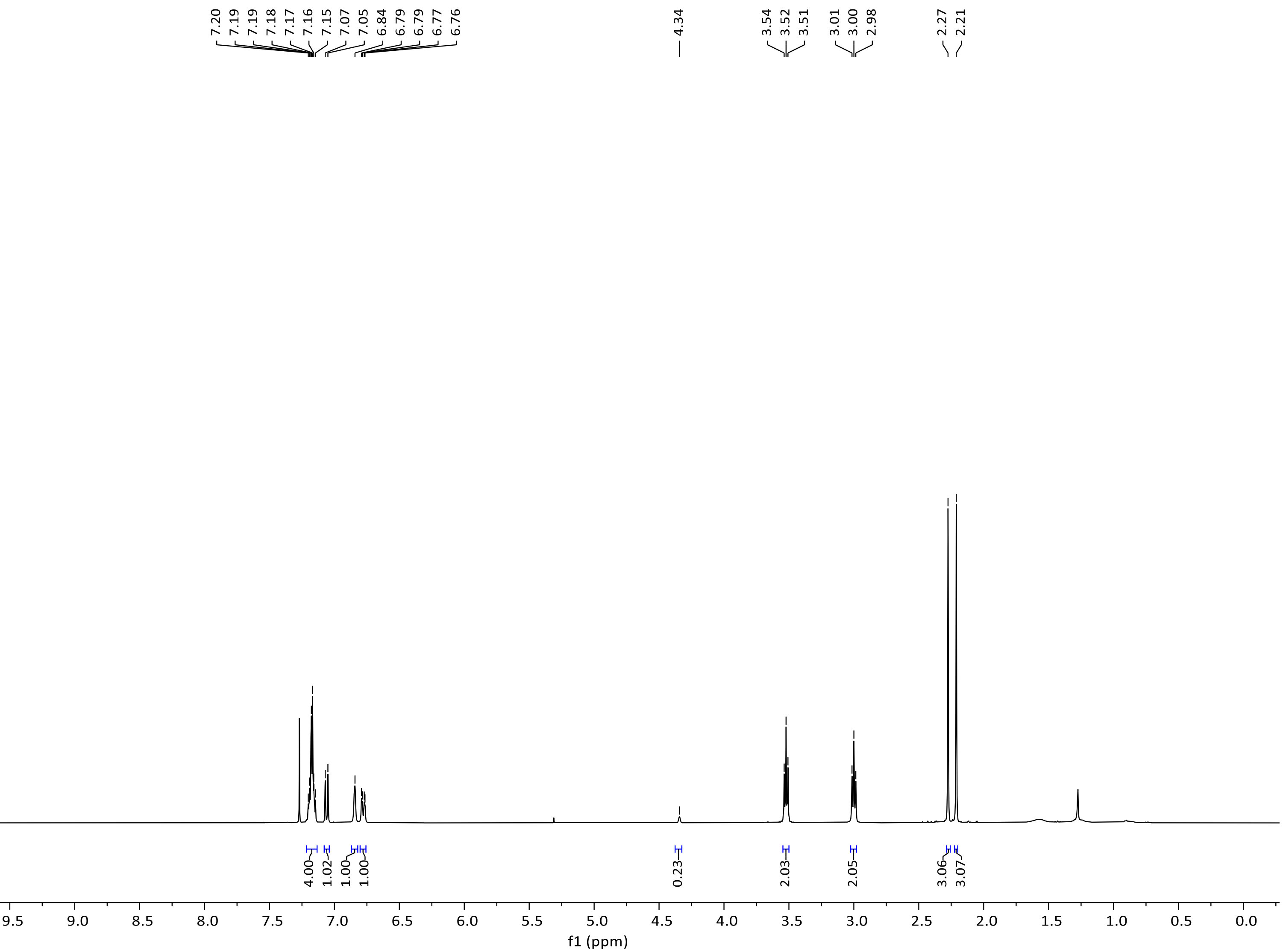
^{1}H NMR spectrum of **5a** (600 MHz, $CDCl_3$)



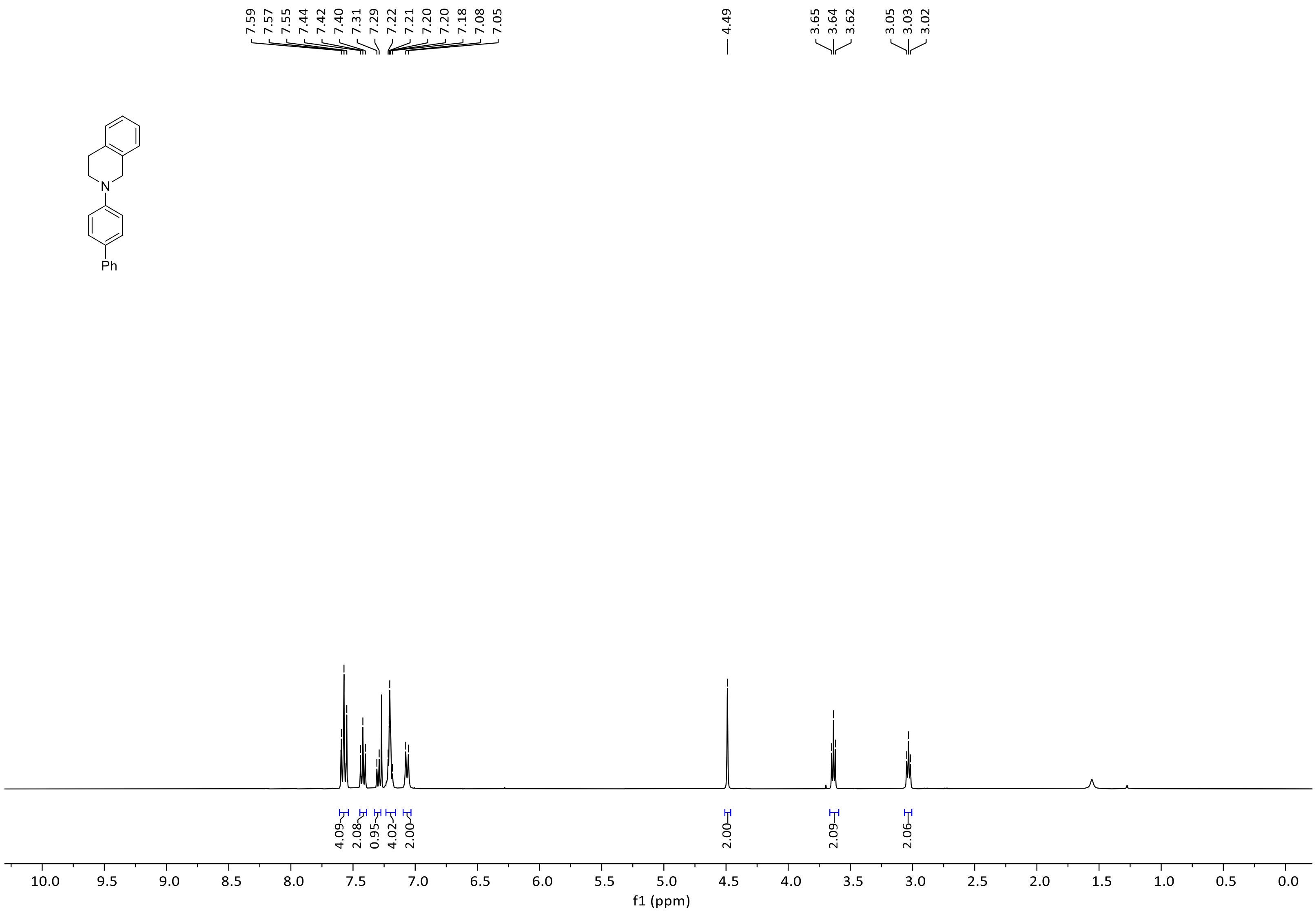


^{1}H NMR spectrum of **06** (600 MHz, $CDCl_3$)

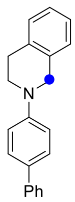


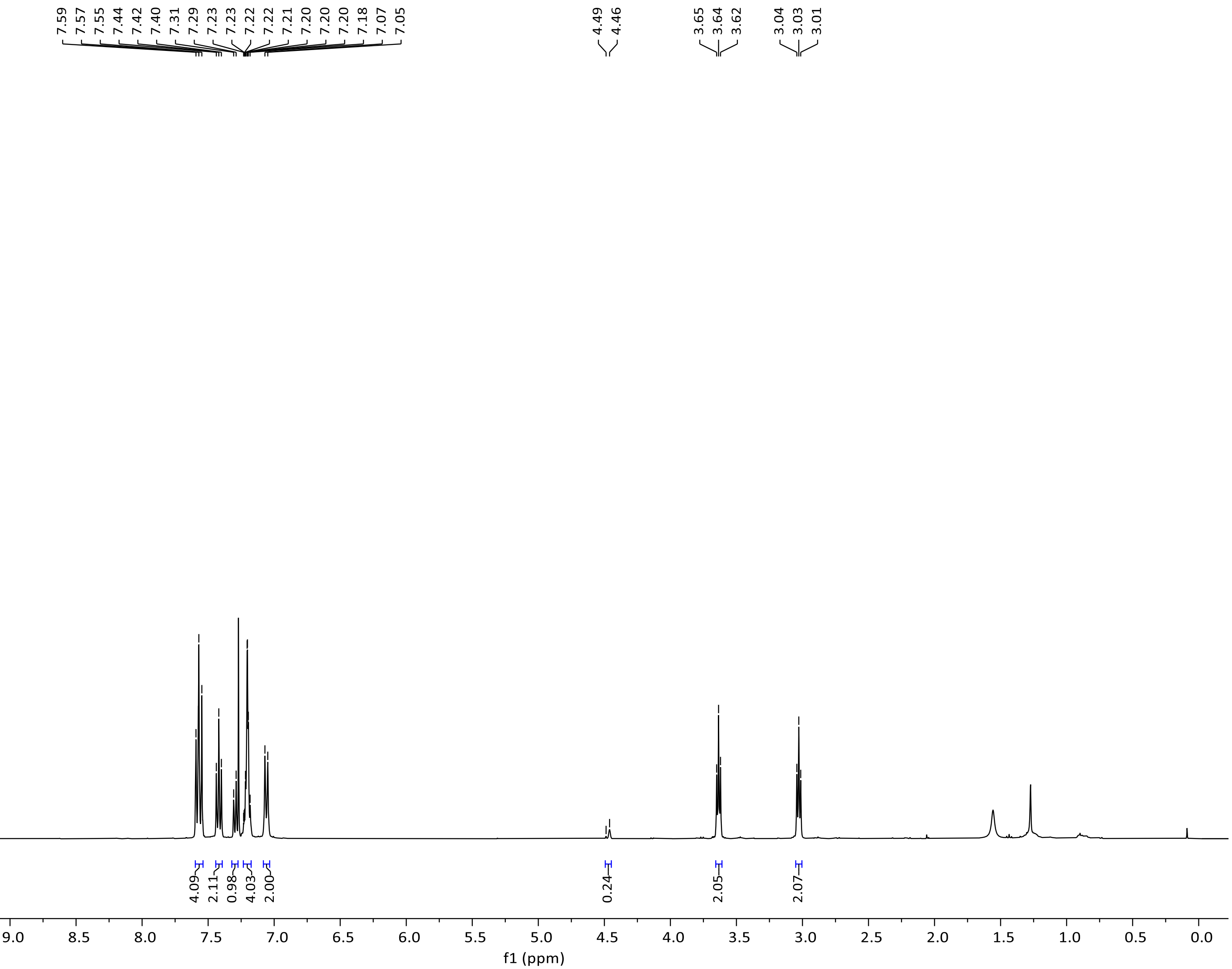


^{1}H NMR spectrum of **6a** (600 MHz, $CDCl_3$)

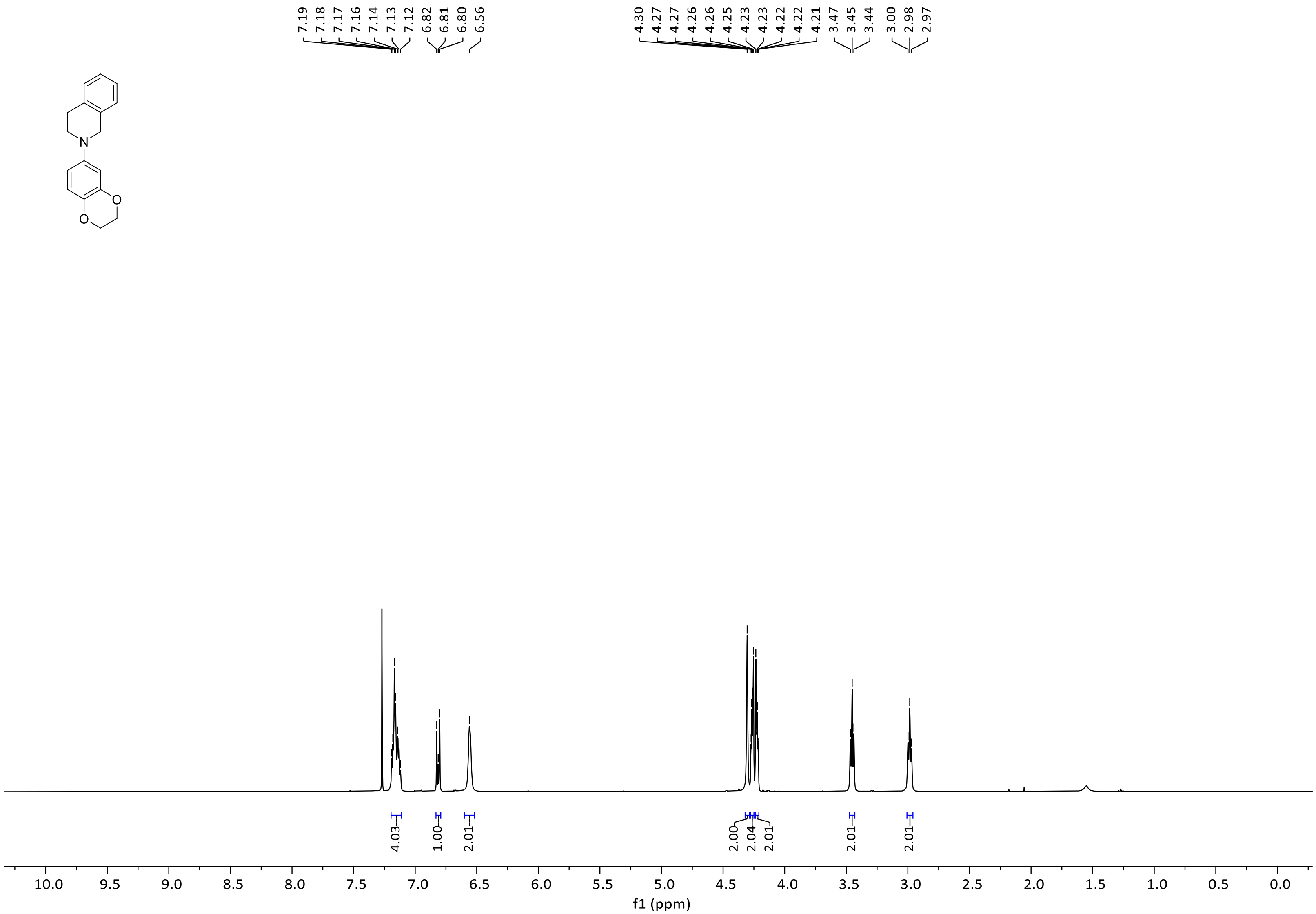


^{1}H NMR spectrum of **07** (600 MHz, $CDCl_3$)

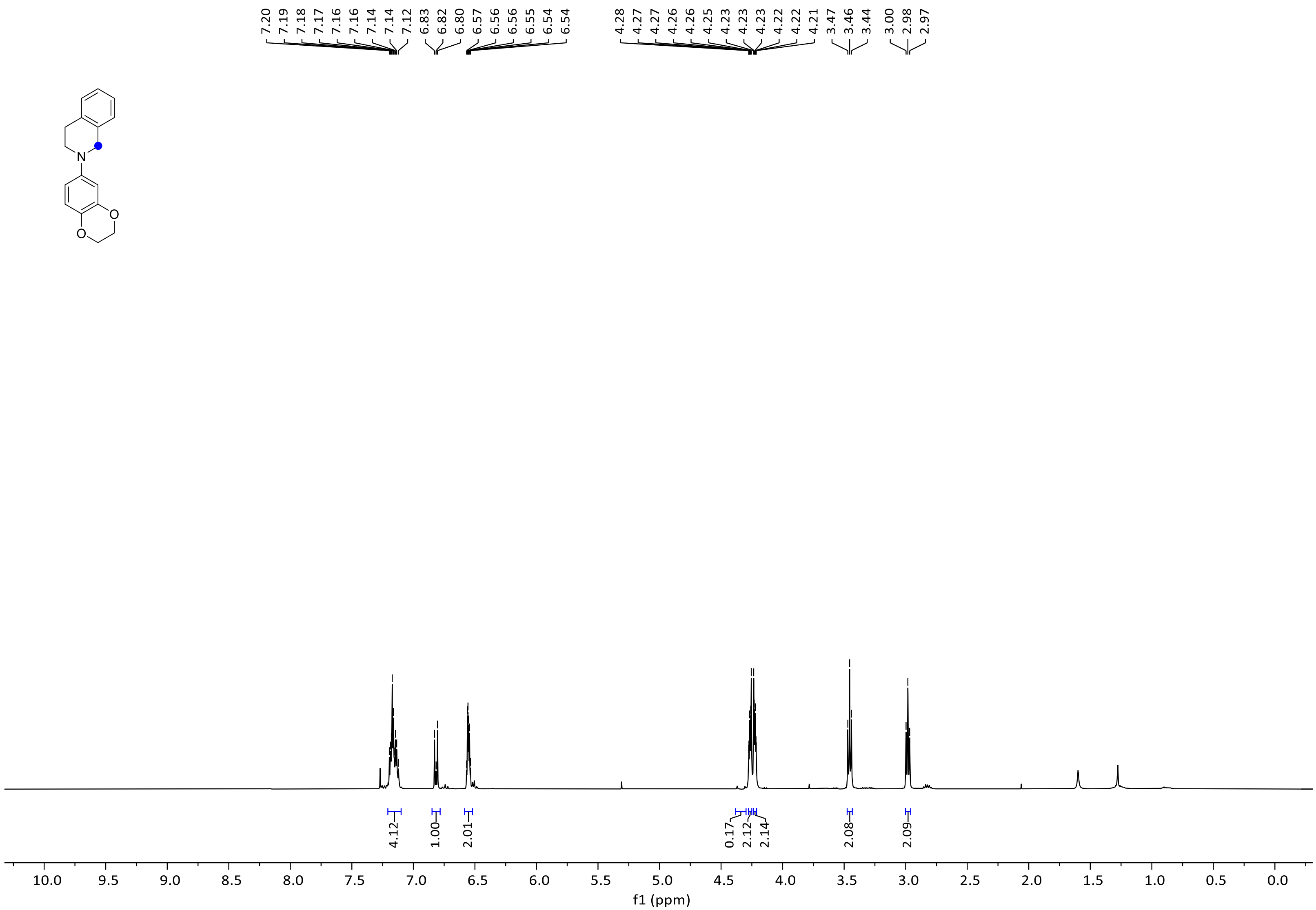




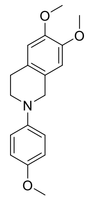
^{1}H NMR spectrum of **7a** (600 MHz, $CDCl_3$)

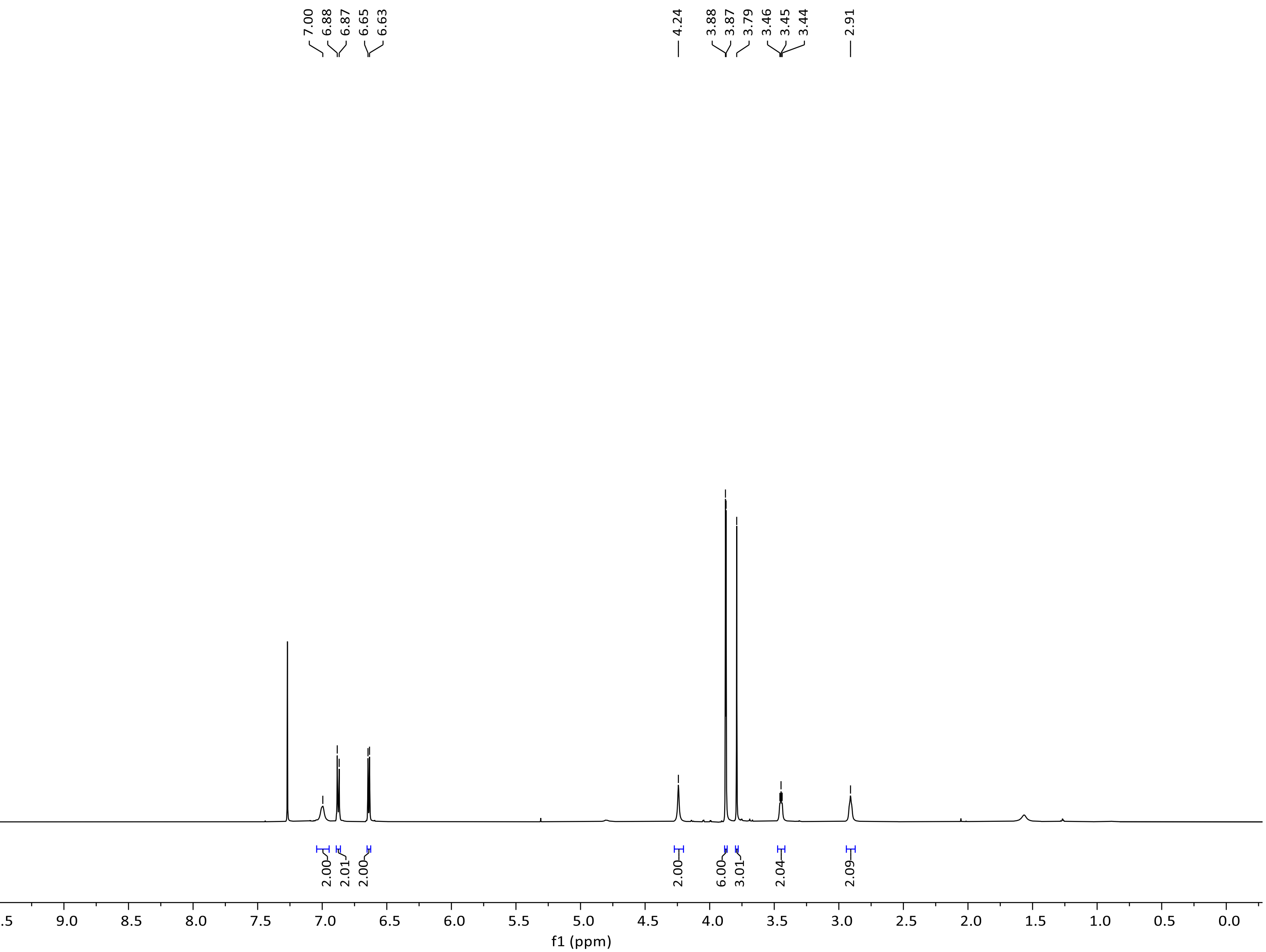


[1]H NMR spectrum of **08** (600 MHz, $CDCl_3$)

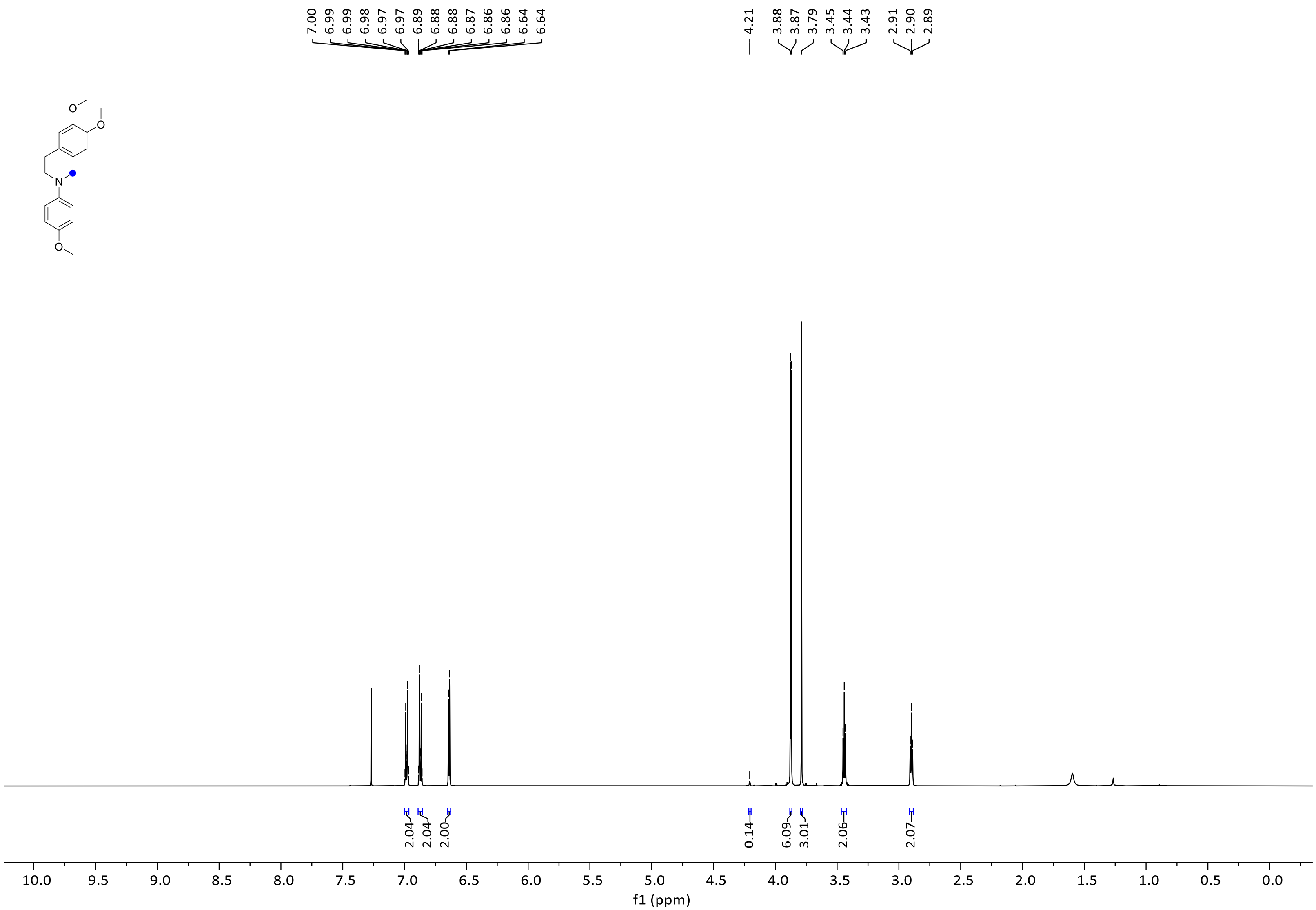


^{1}H NMR spectrum of **8a** (600 MHz, $CDCl_3$)

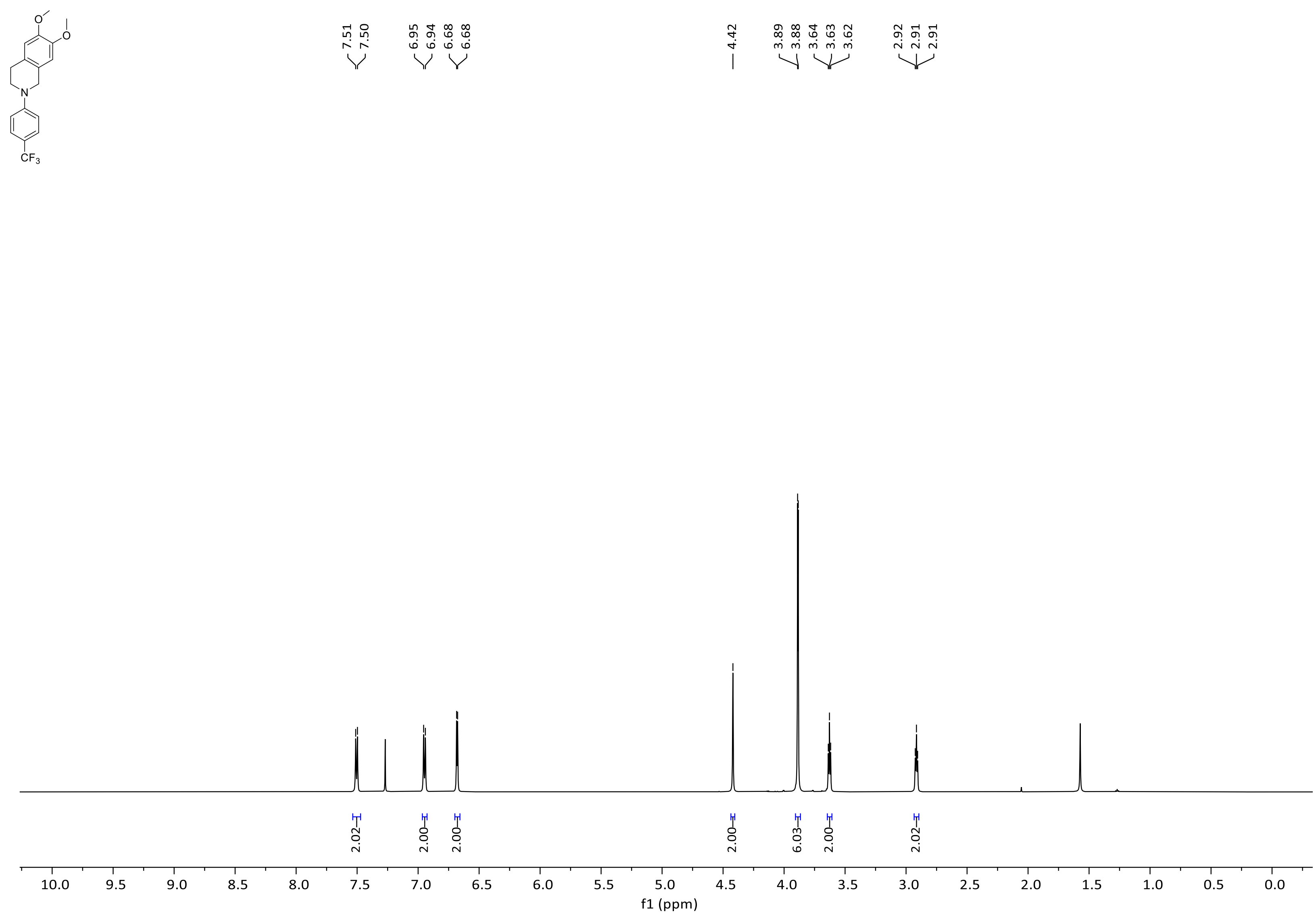




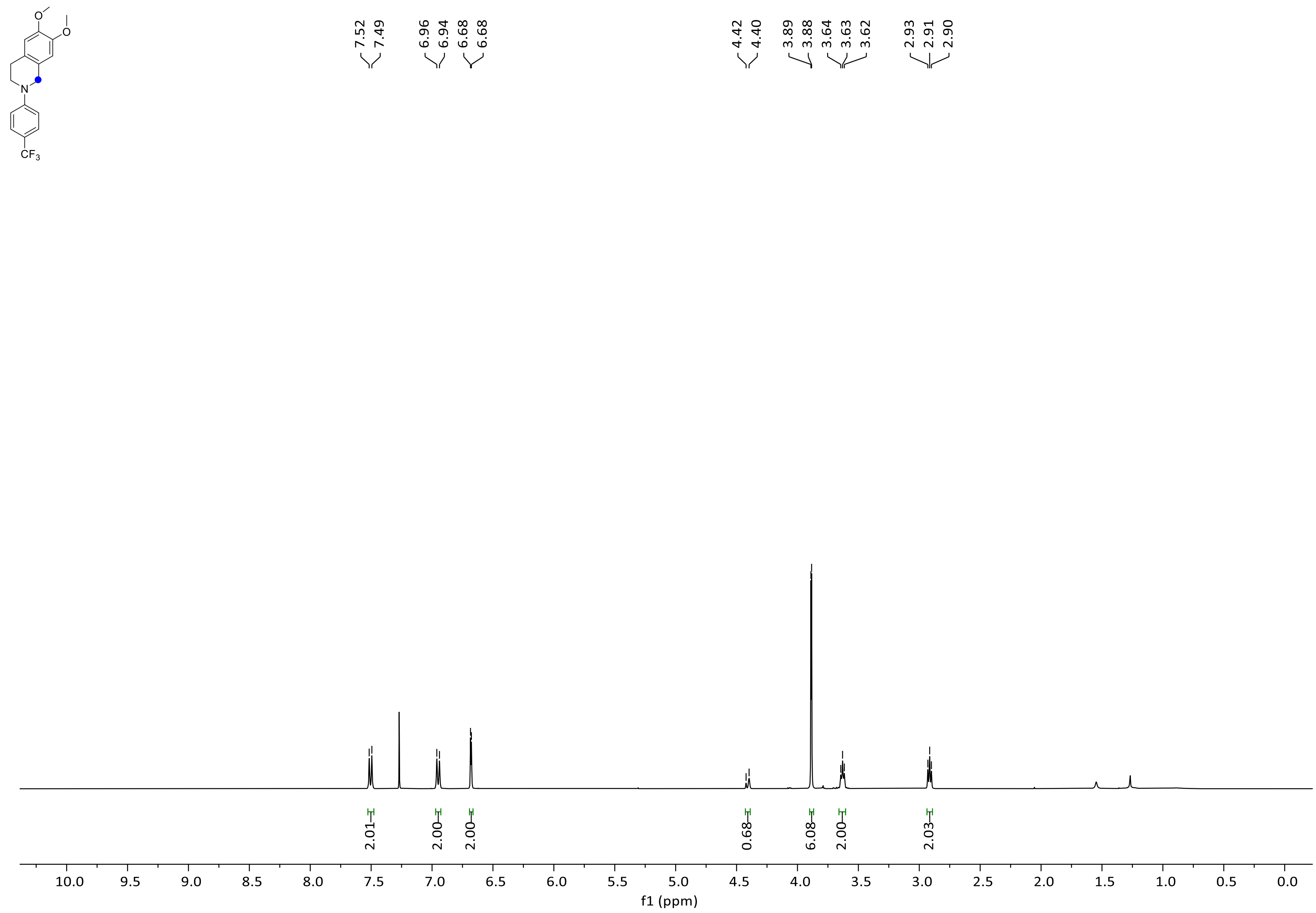
^{1}H NMR spectrum of **09** (600 MHz, $CDCl_3$)



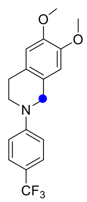
^{1}H NMR spectrum of **9a** (600 MHz, $CDCl_3$)

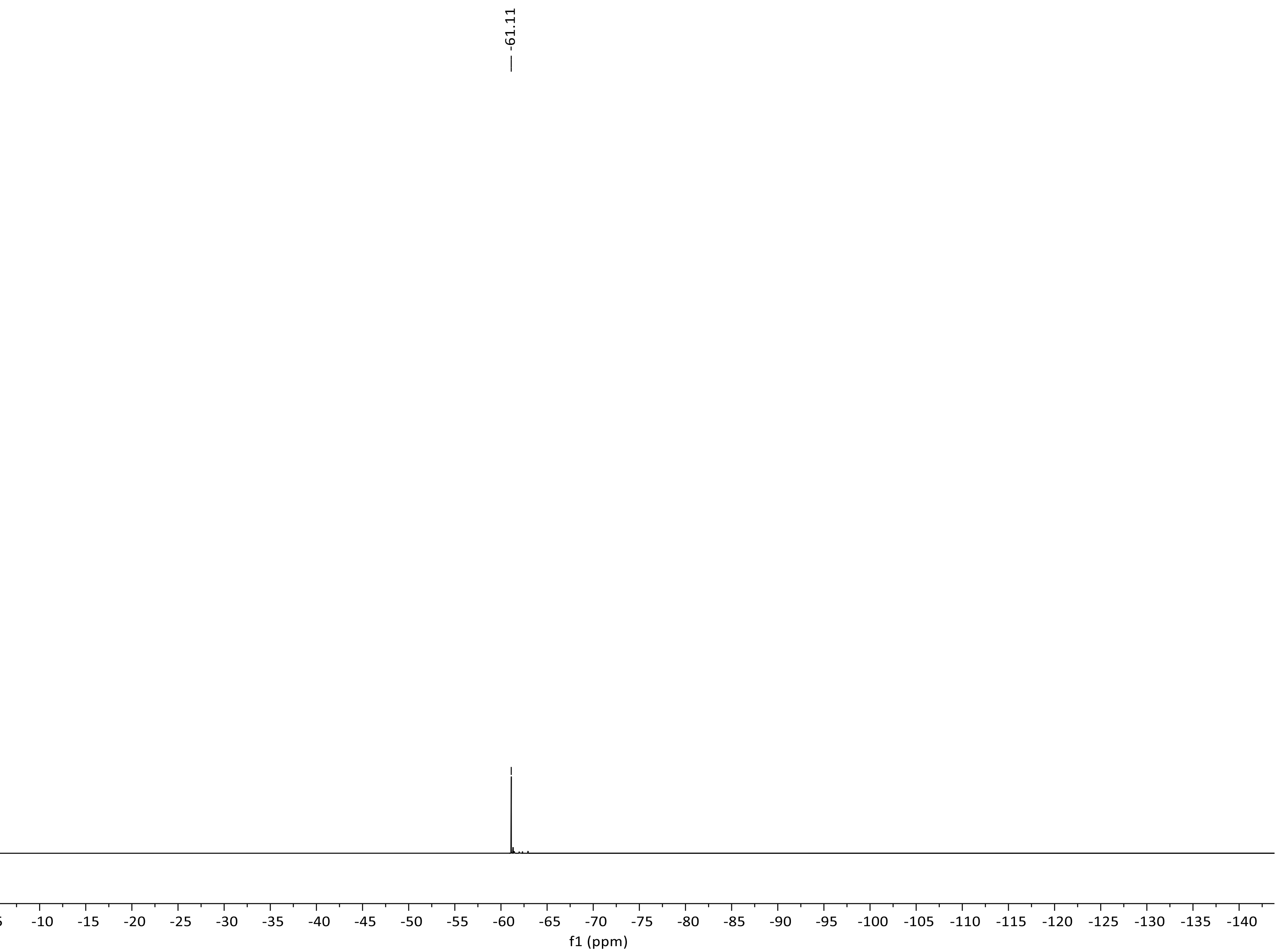


^{1}H NMR spectrum of **10** (600 MHz, $CDCl_3$)

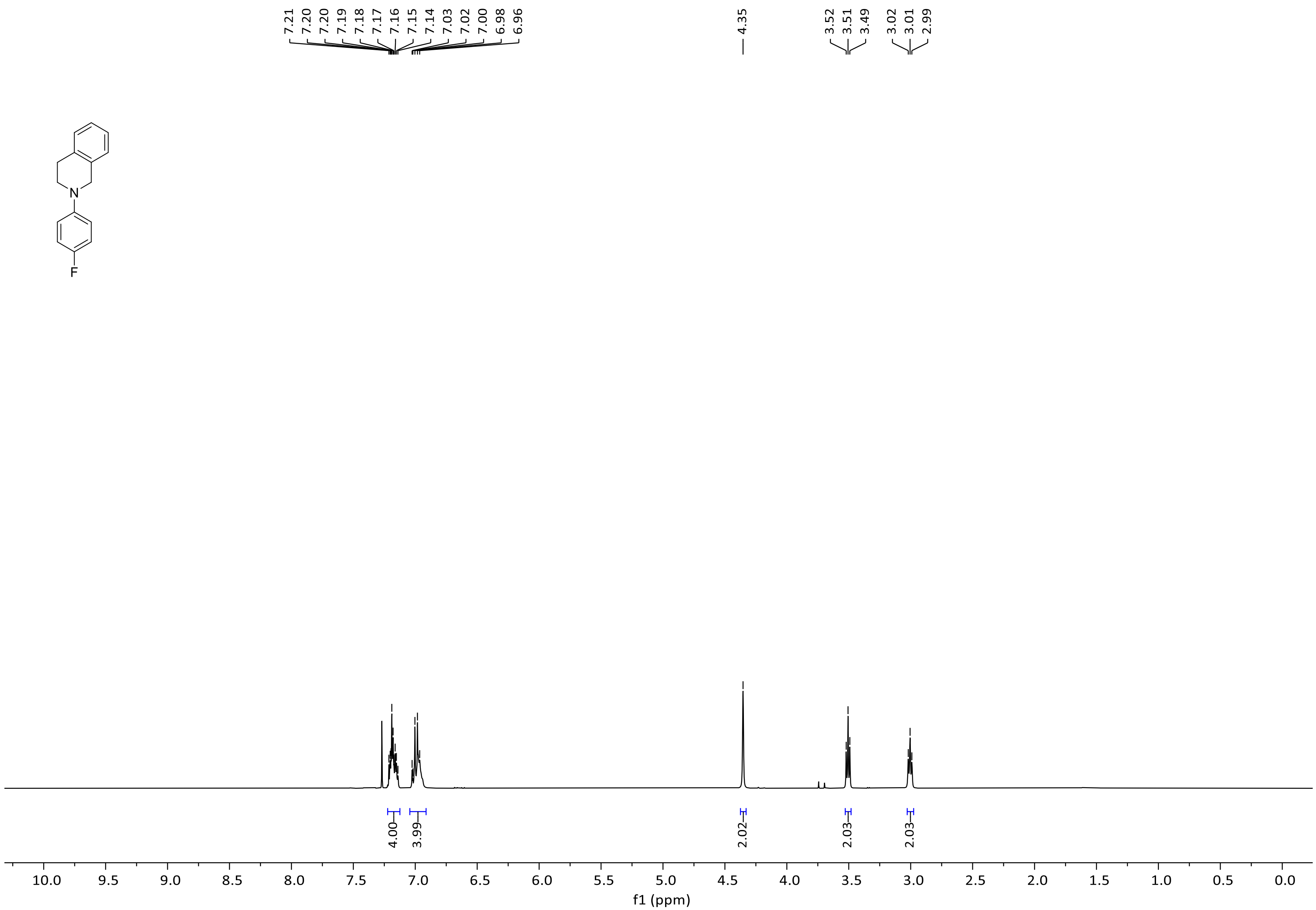


^{1}H NMR spectrum of **10a** (600 MHz, $CDCl_3$)

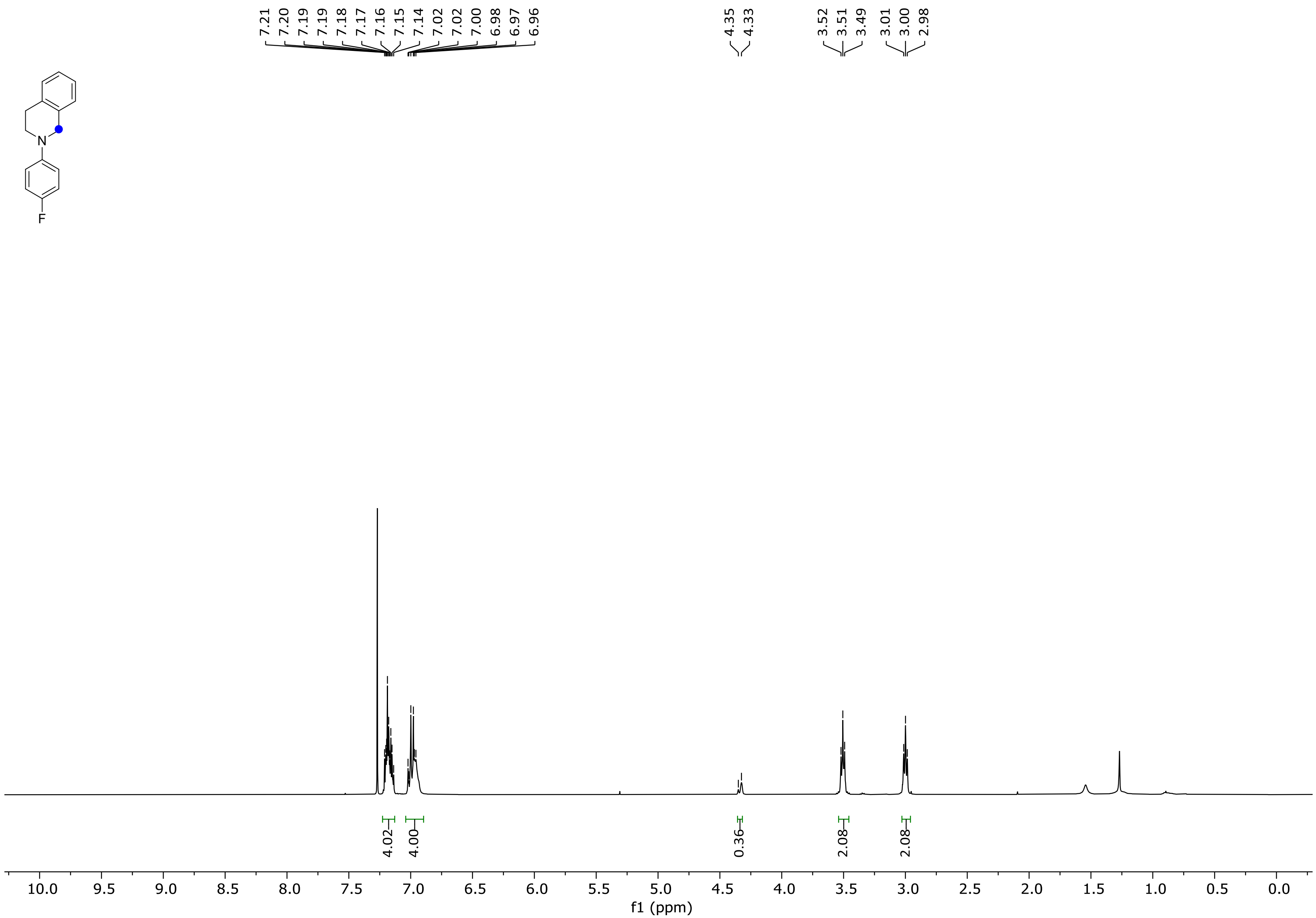




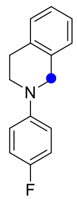
[19]F NMR spectrum of **10a** (471 MHz, $CDCl_3$)

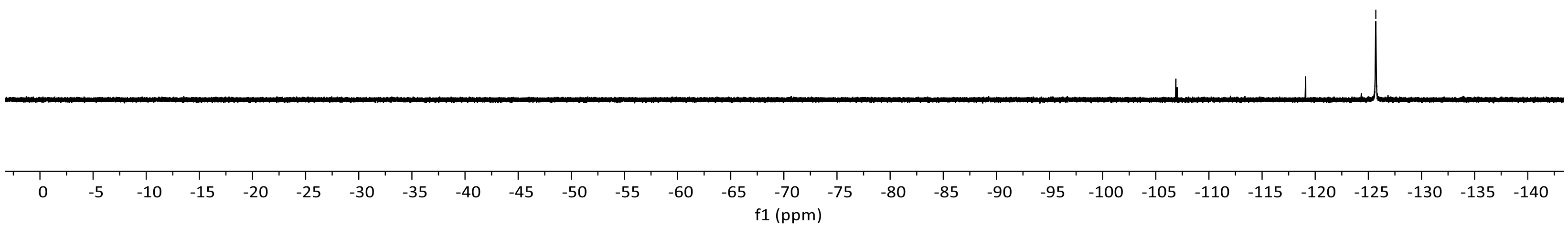


^{1}H NMR spectrum of **11** (600 MHz, $CDCl_3$)

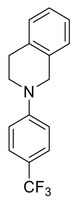


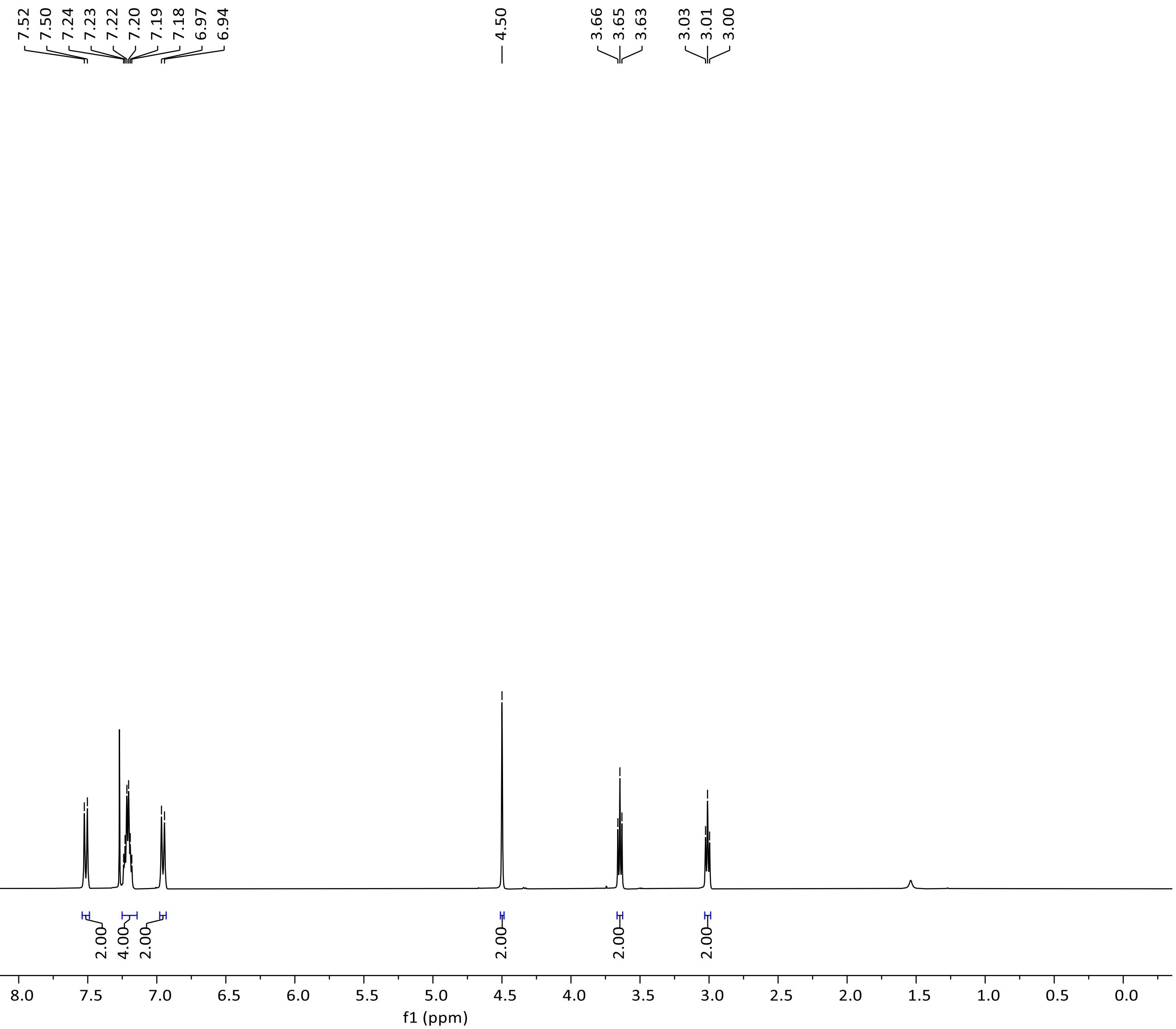
^{1}H NMR spectrum of **11a** (600 MHz, $CDCl_3$)



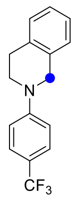


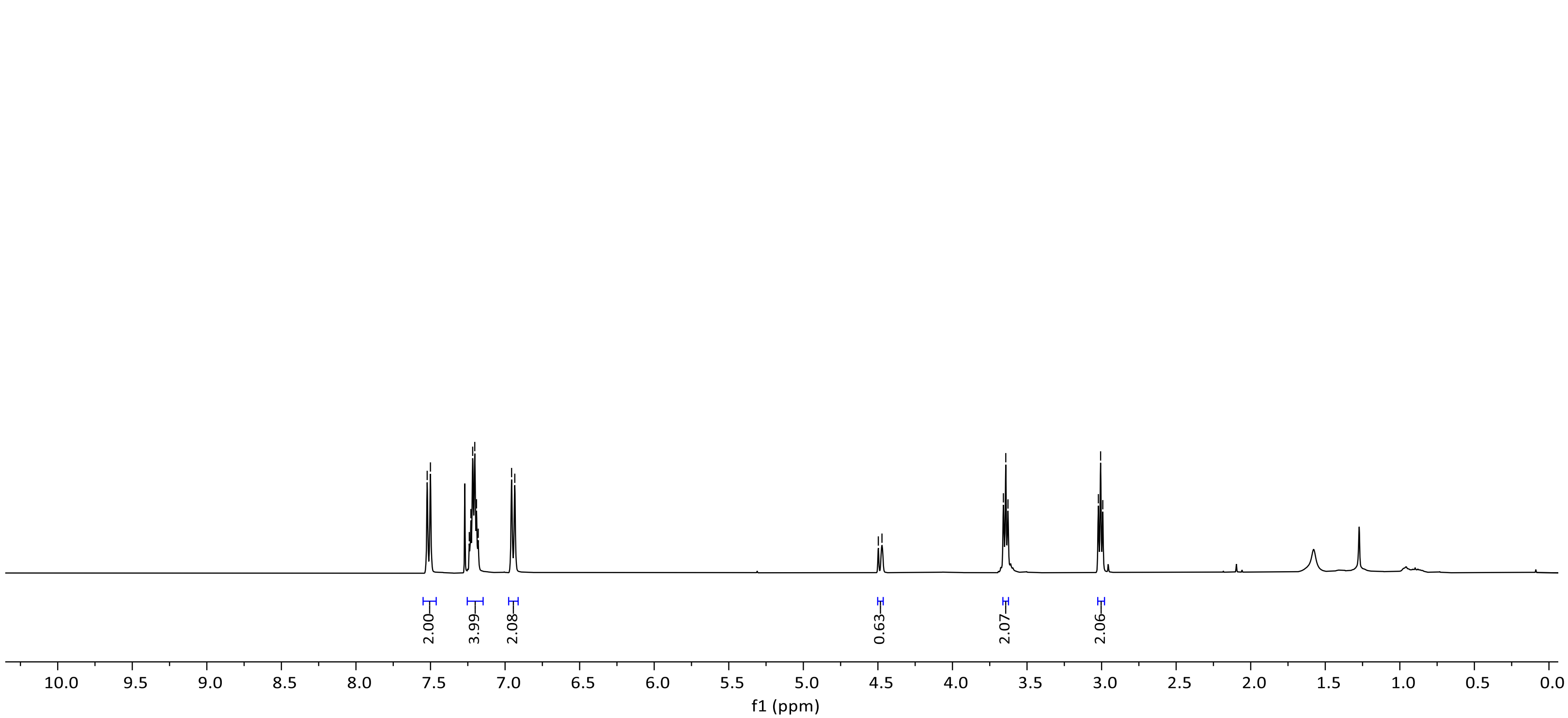
^{19}F NMR spectrum of **11a** (471 MHz, $CDCl_3$)



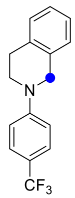


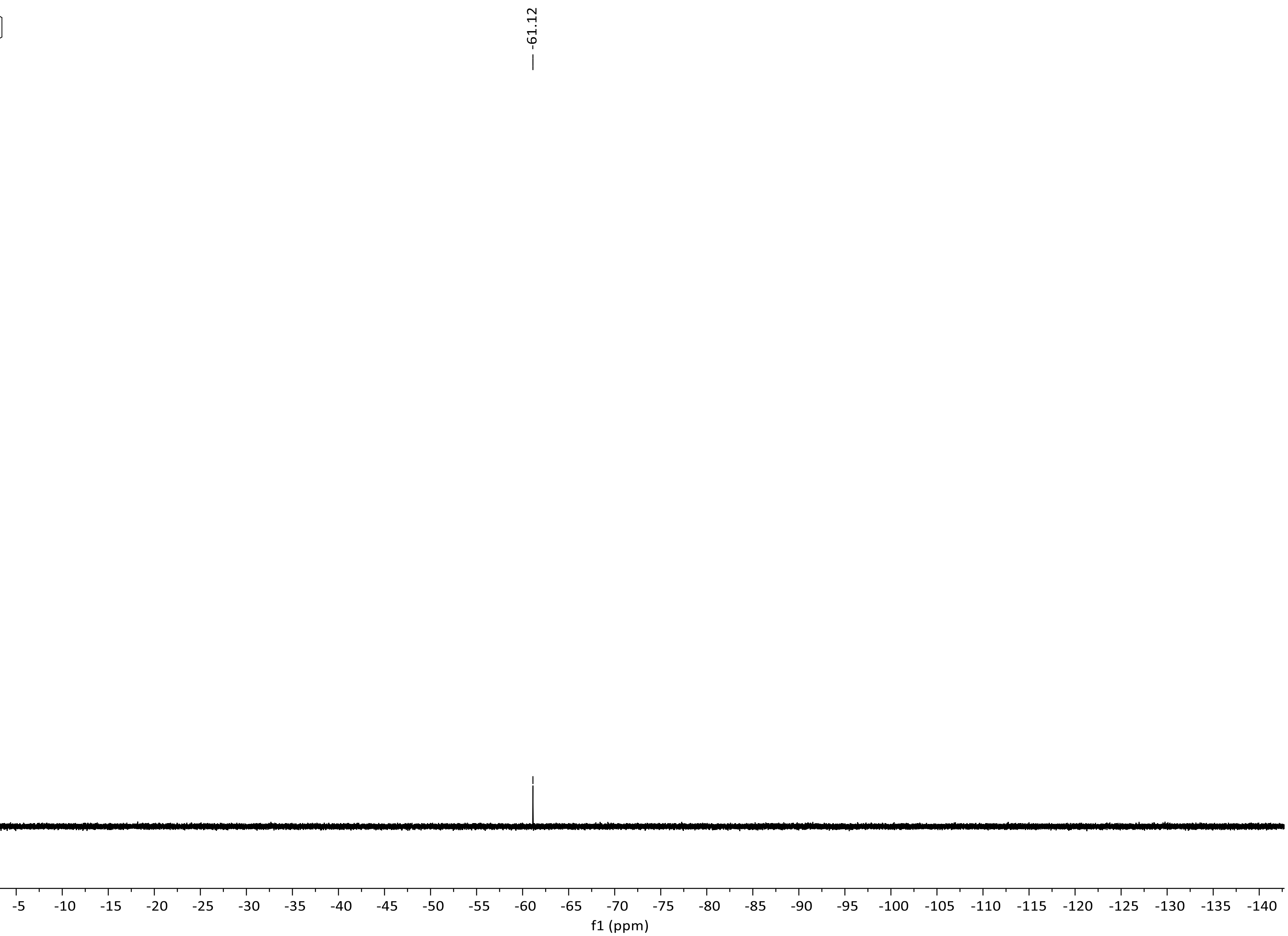
^{1}H NMR spectrum of **12** (600 MHz, $CDCl_3$)



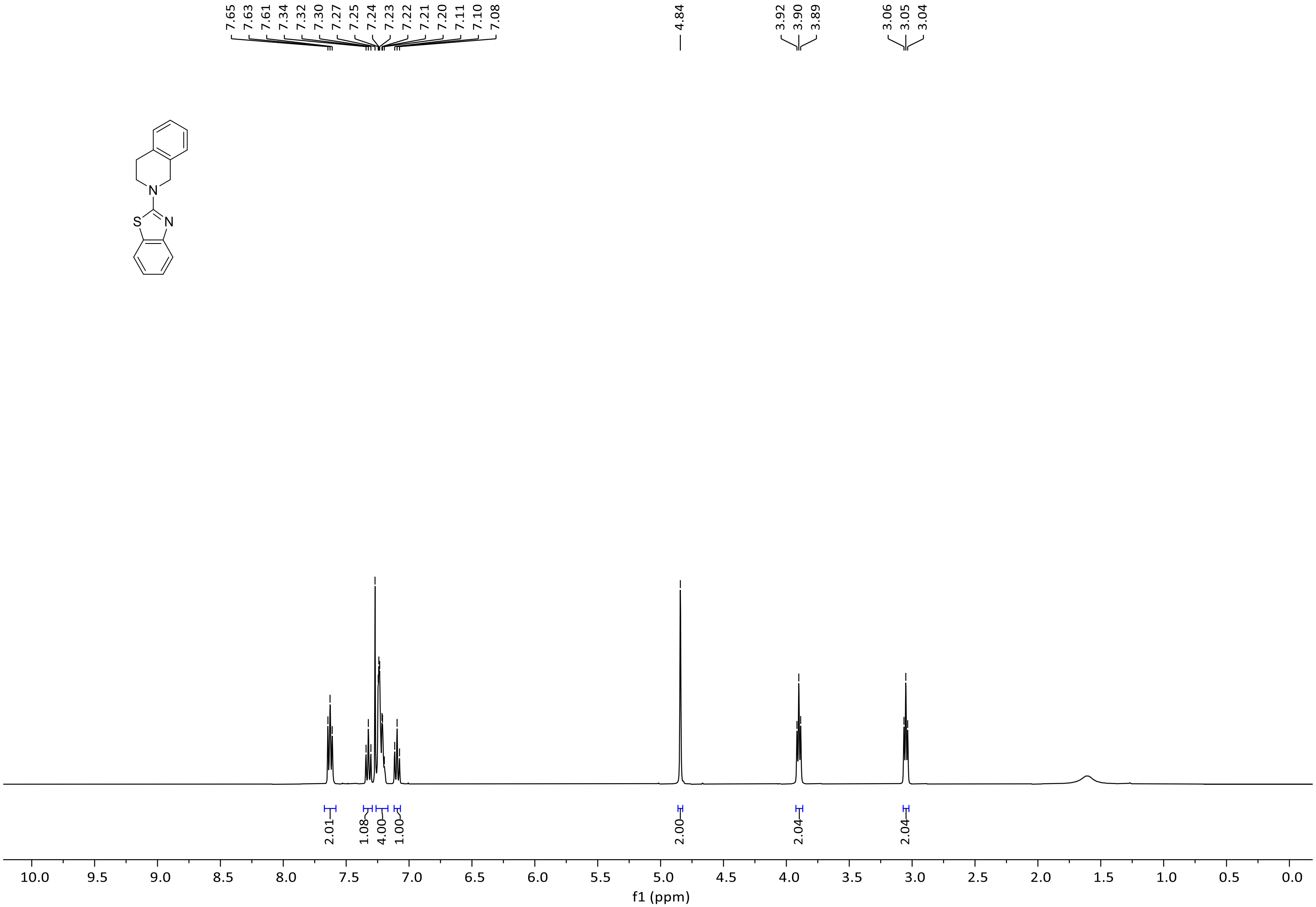


^{1}H NMR spectrum of **12a** (600 MHz, $CDCl_3$)

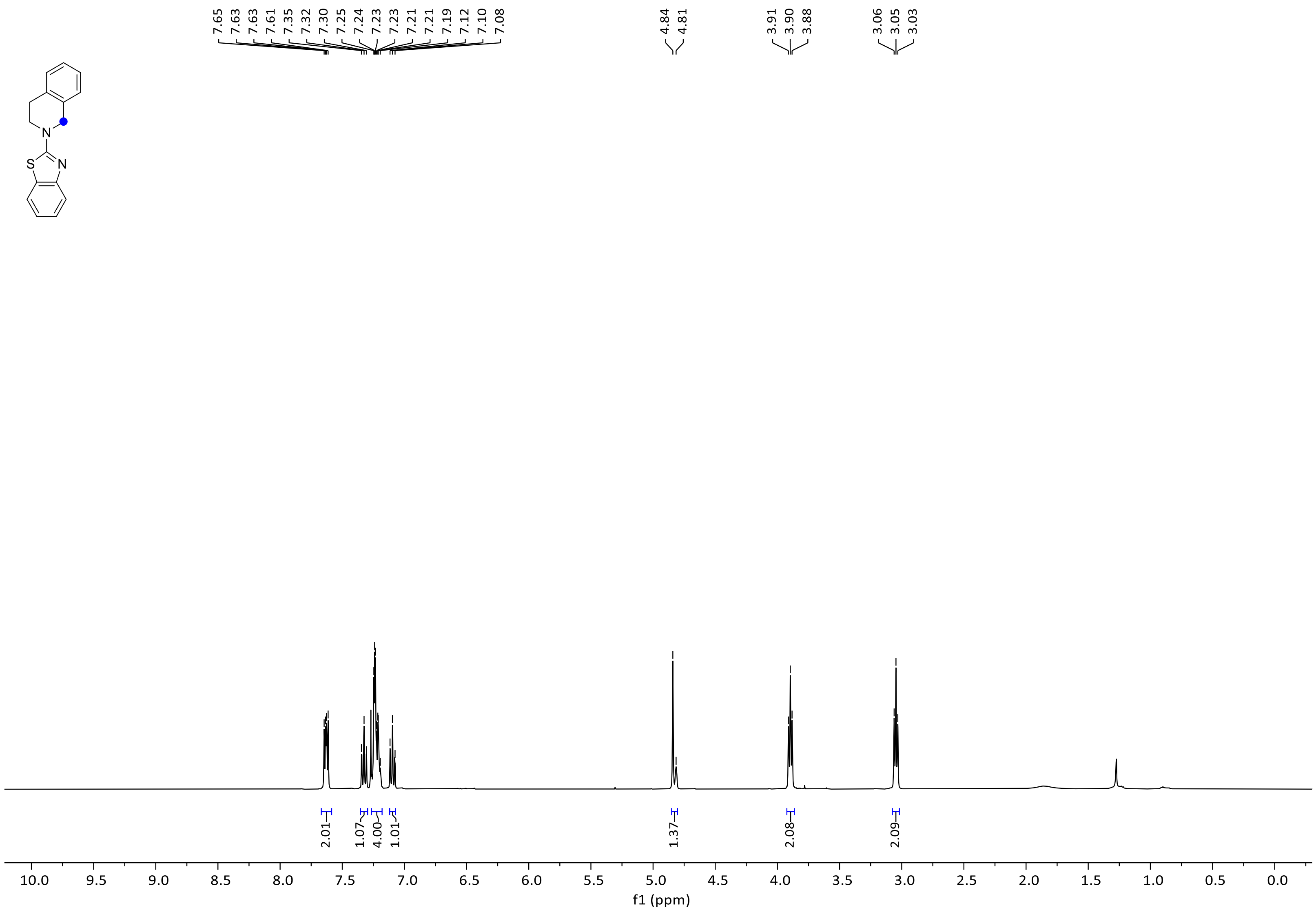




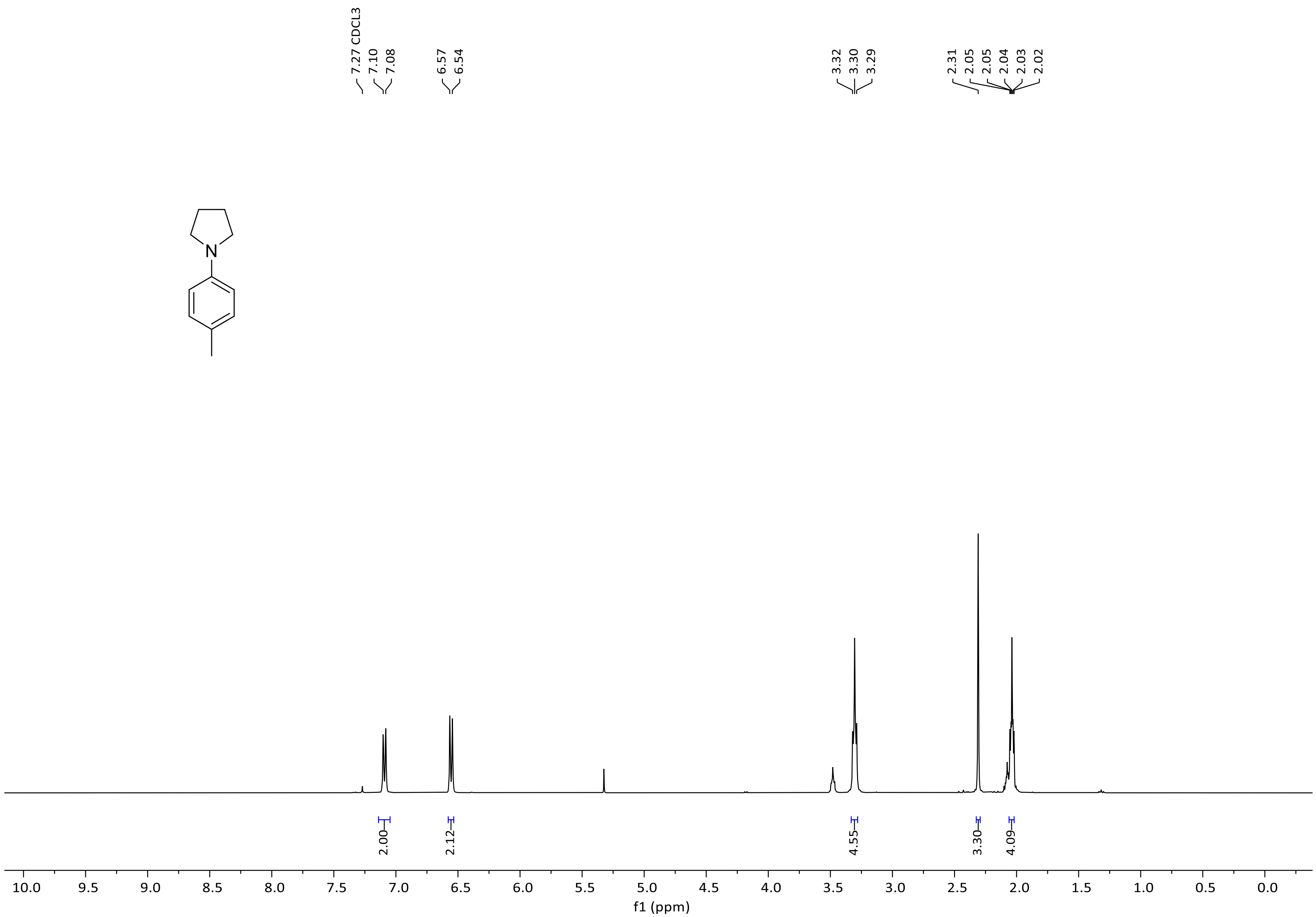
^{19}F NMR spectrum of **12a** (376 MHz, $CDCl_3$)



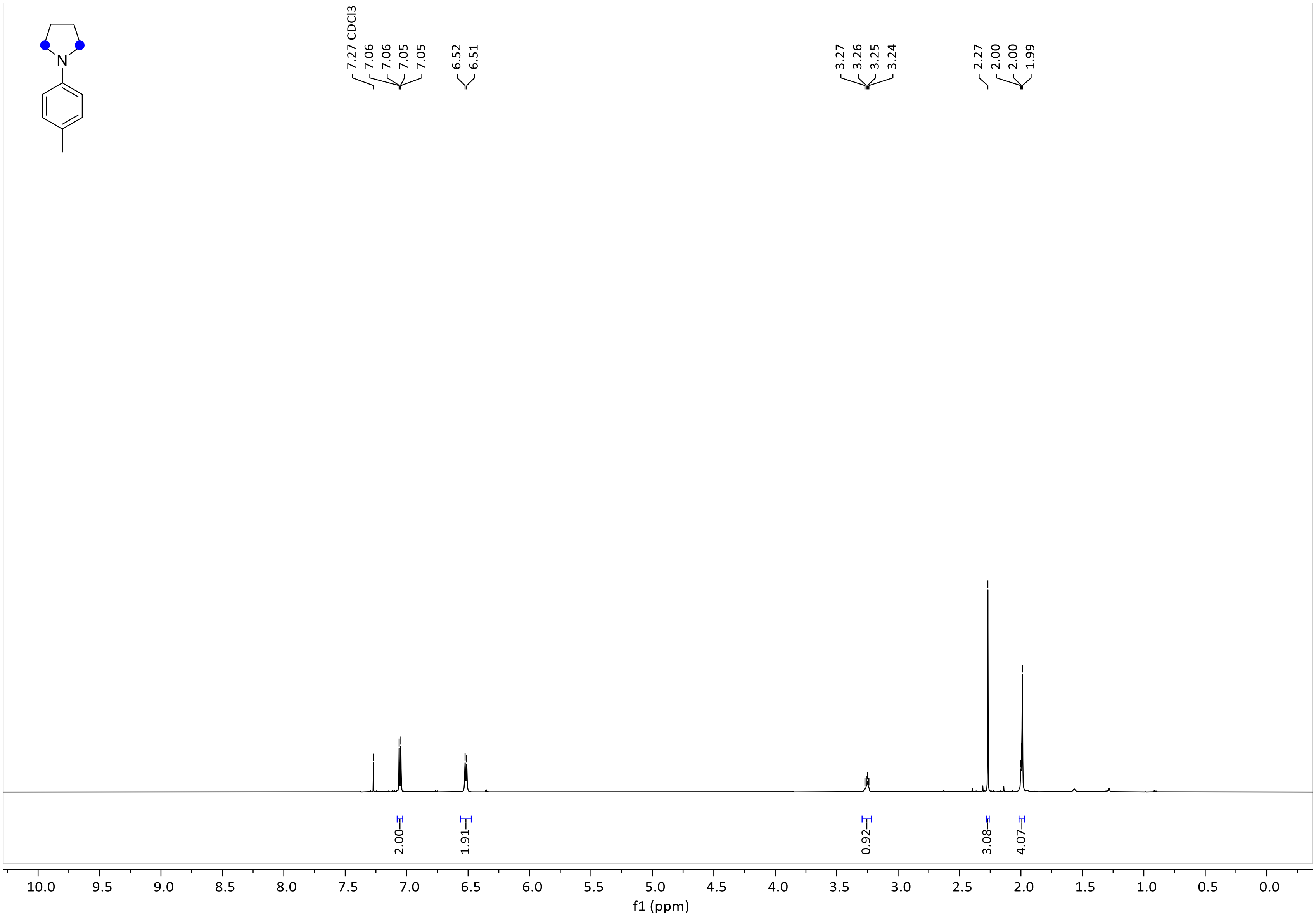
^{1}H NMR spectrum of **13** (600 MHz, $CDCl_3$)



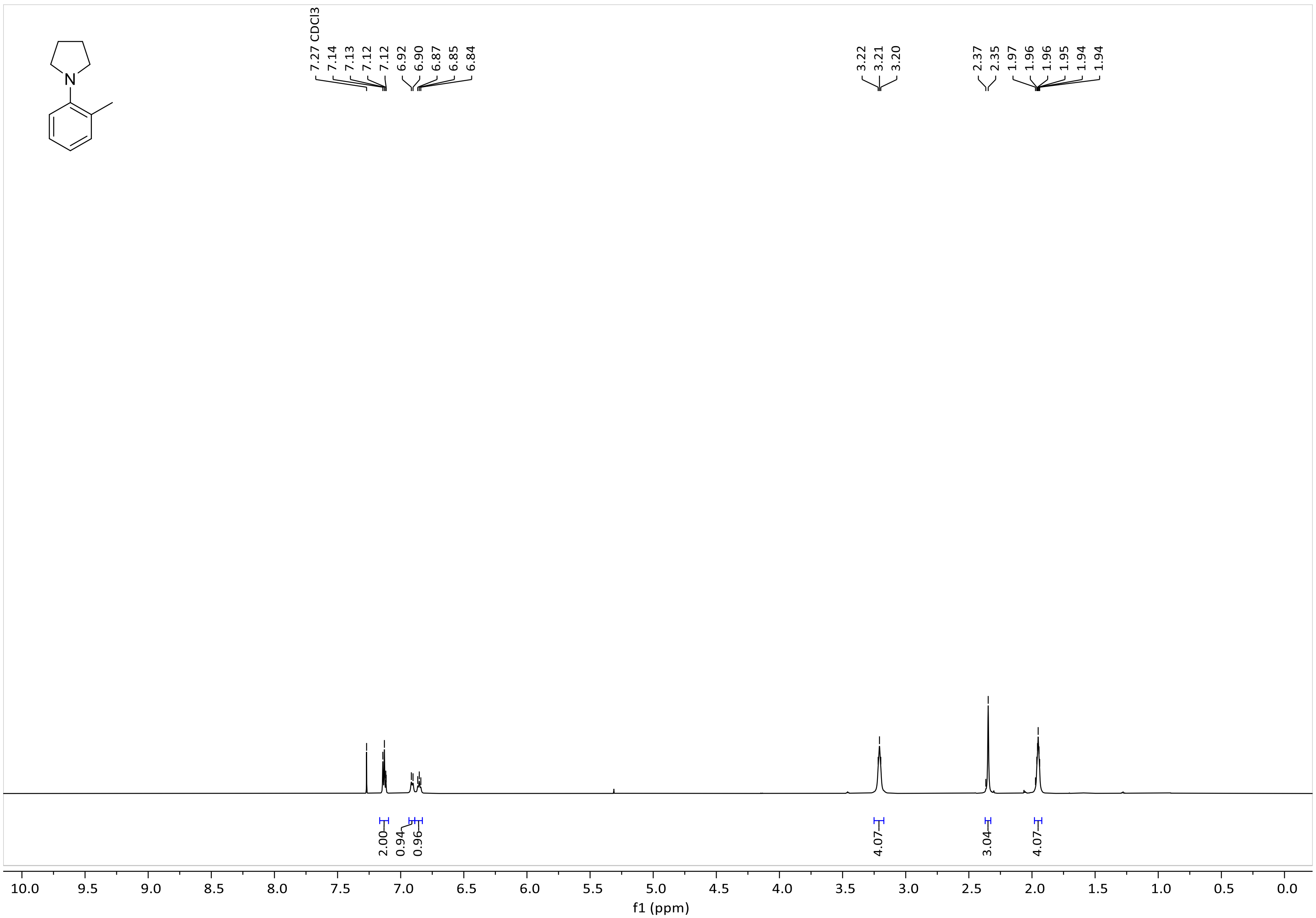
^1H NMR spectrum of **13a** (600 MHz, $CDCl_3$)



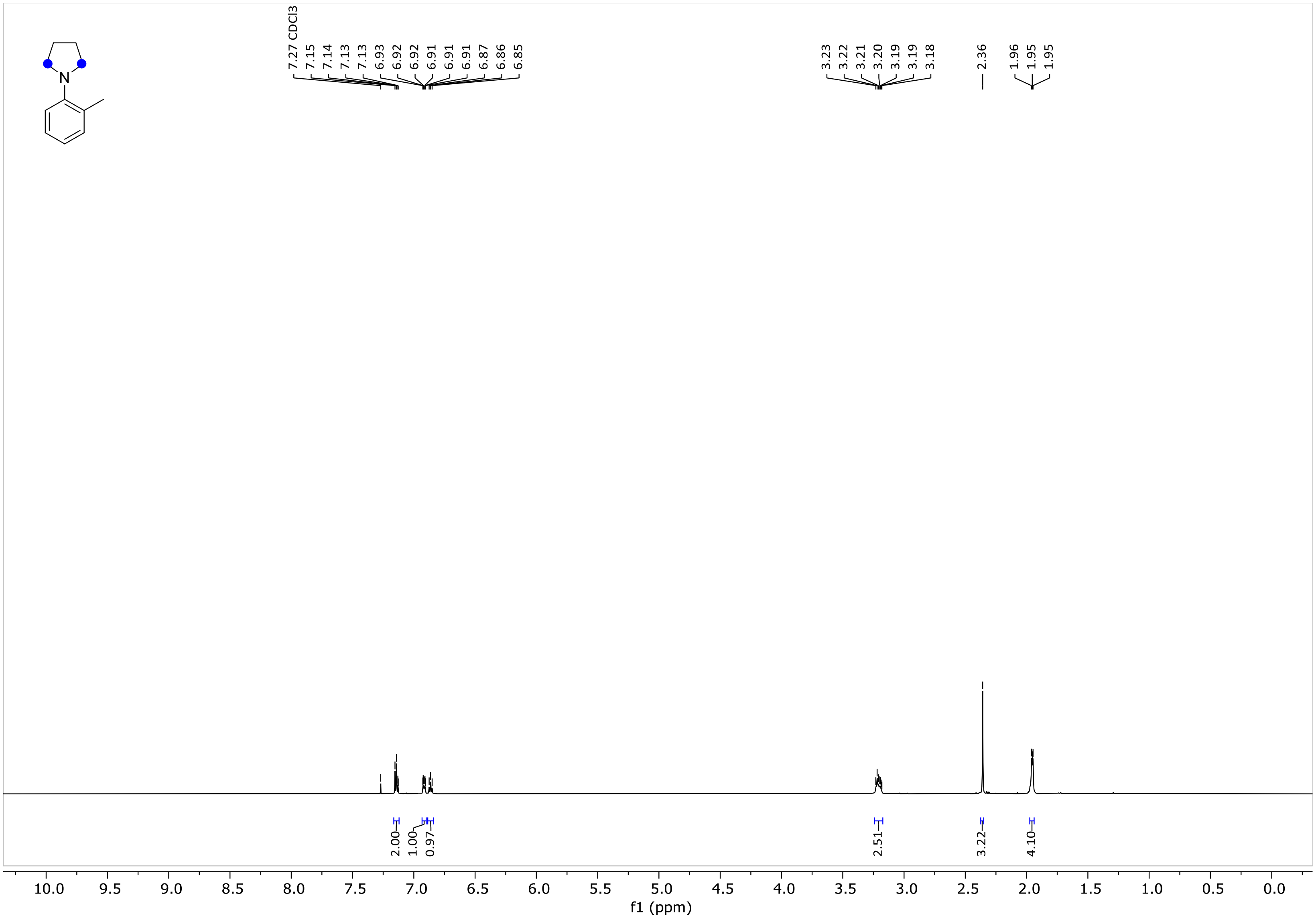
^{1}H NMR spectrum of **14** (600 MHz, $CDCl_3$)



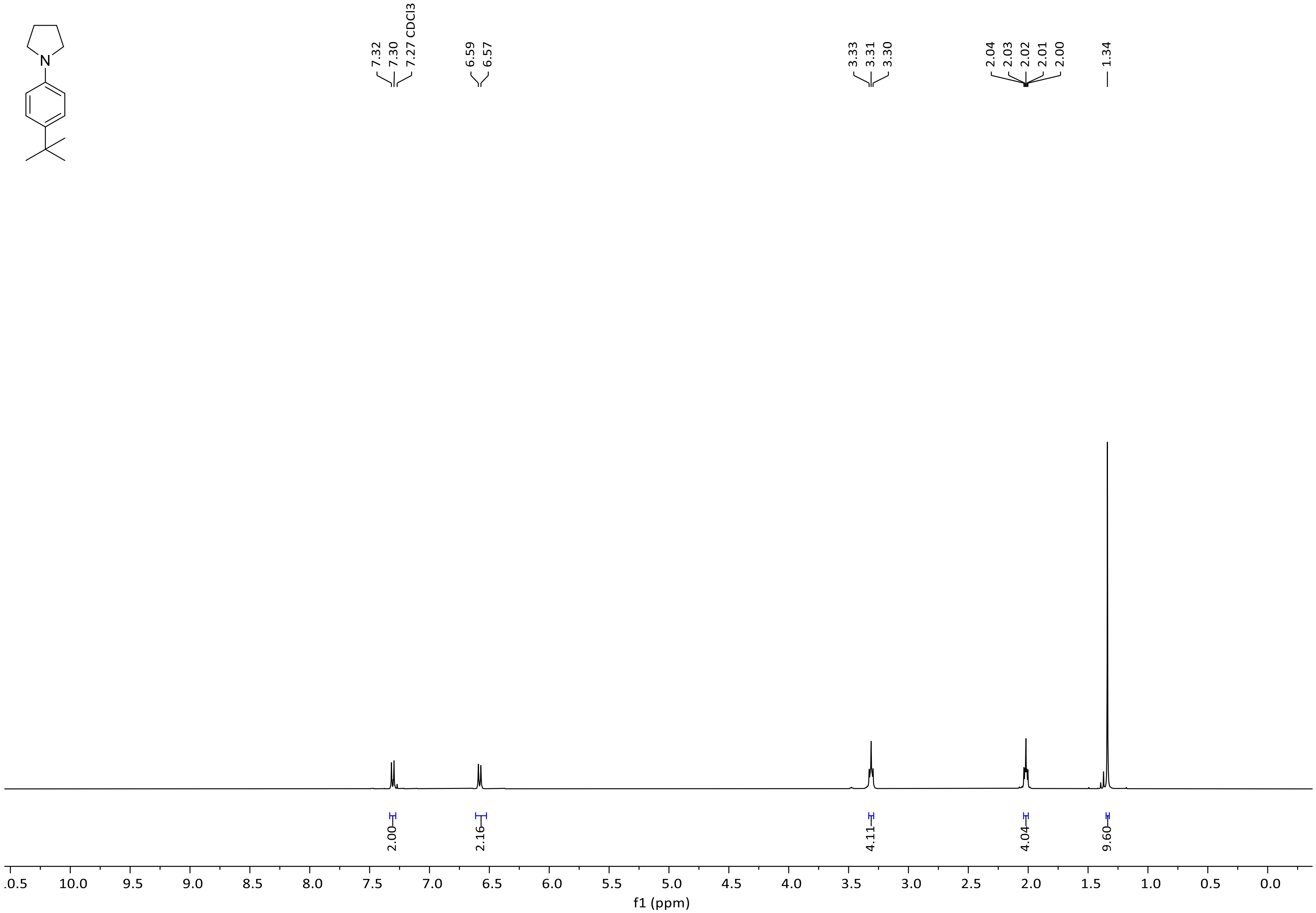
^{1}H NMR spectrum of **14a** (600MHz, $CDCl_3$)



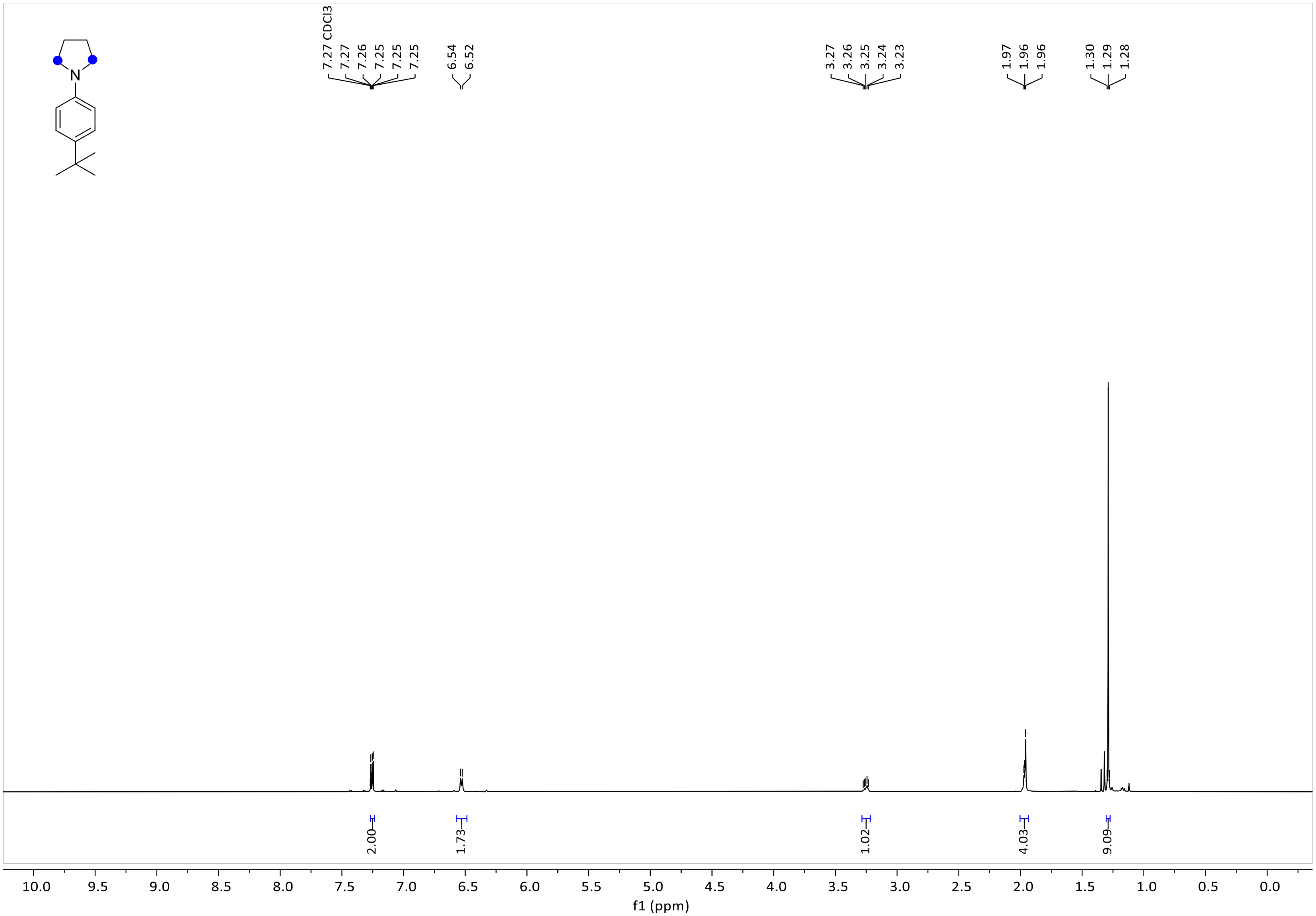
^{1}H NMR spectrum of **15** (600 MHz, $CDCl_3$)



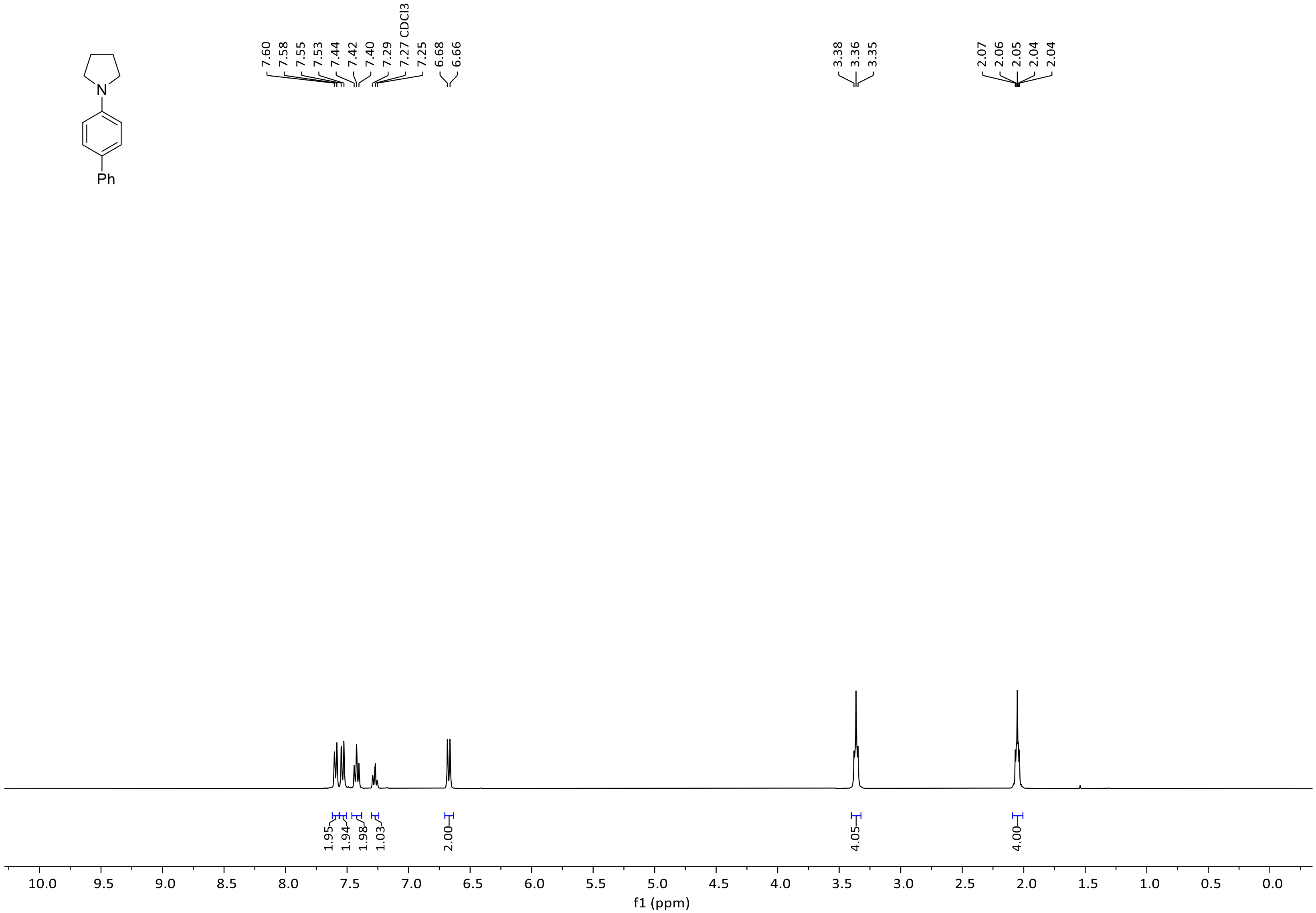
^{1}H NMR spectrum of **15a** (600 MHz, $CDCl_3$)



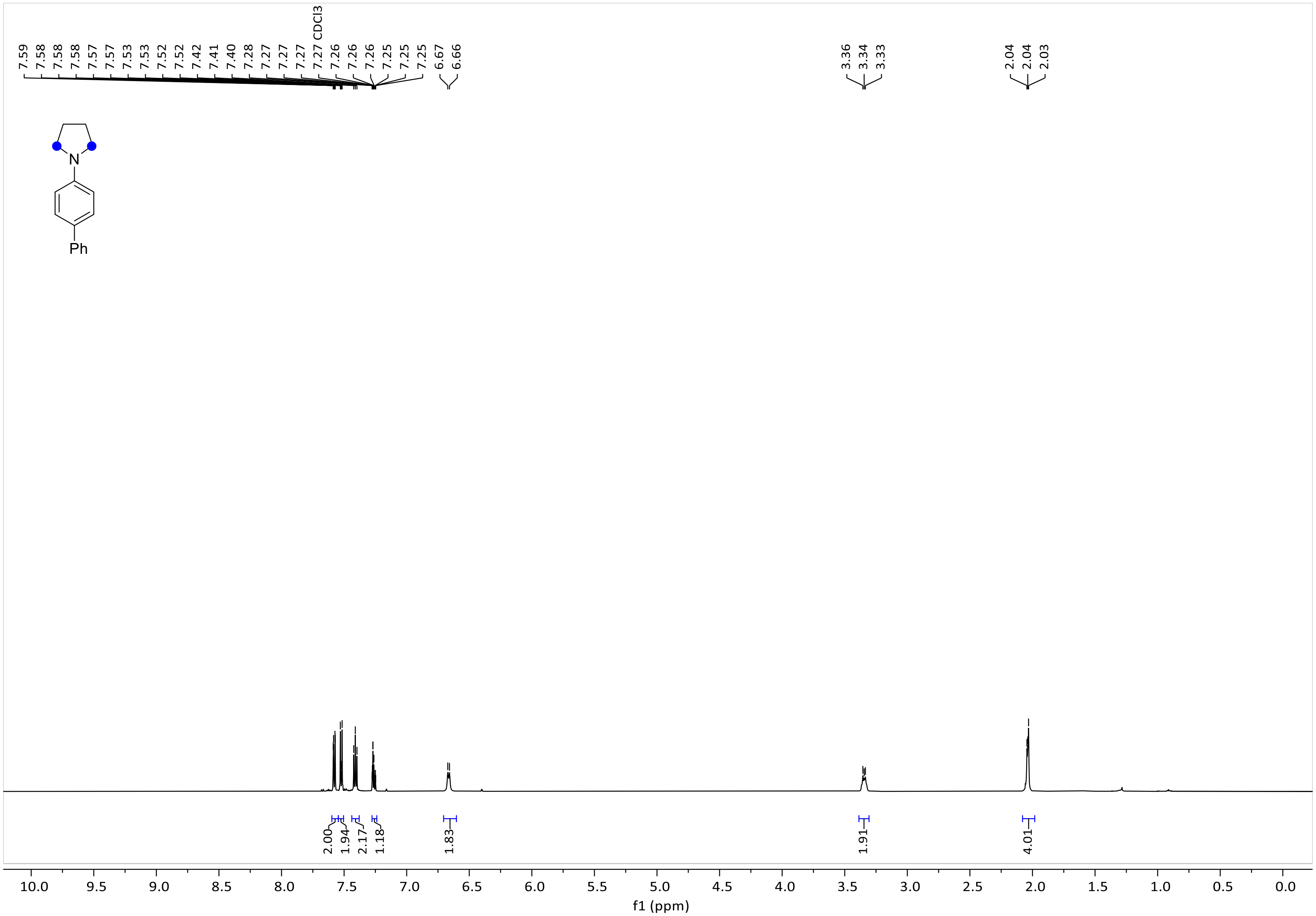
^{1}H NMR spectrum of **16** (600 MHz, $CDCl_3$)



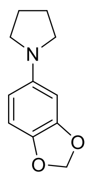
^1H NMR spectrum of **16a** (600 MHz, $CDCl_3$)

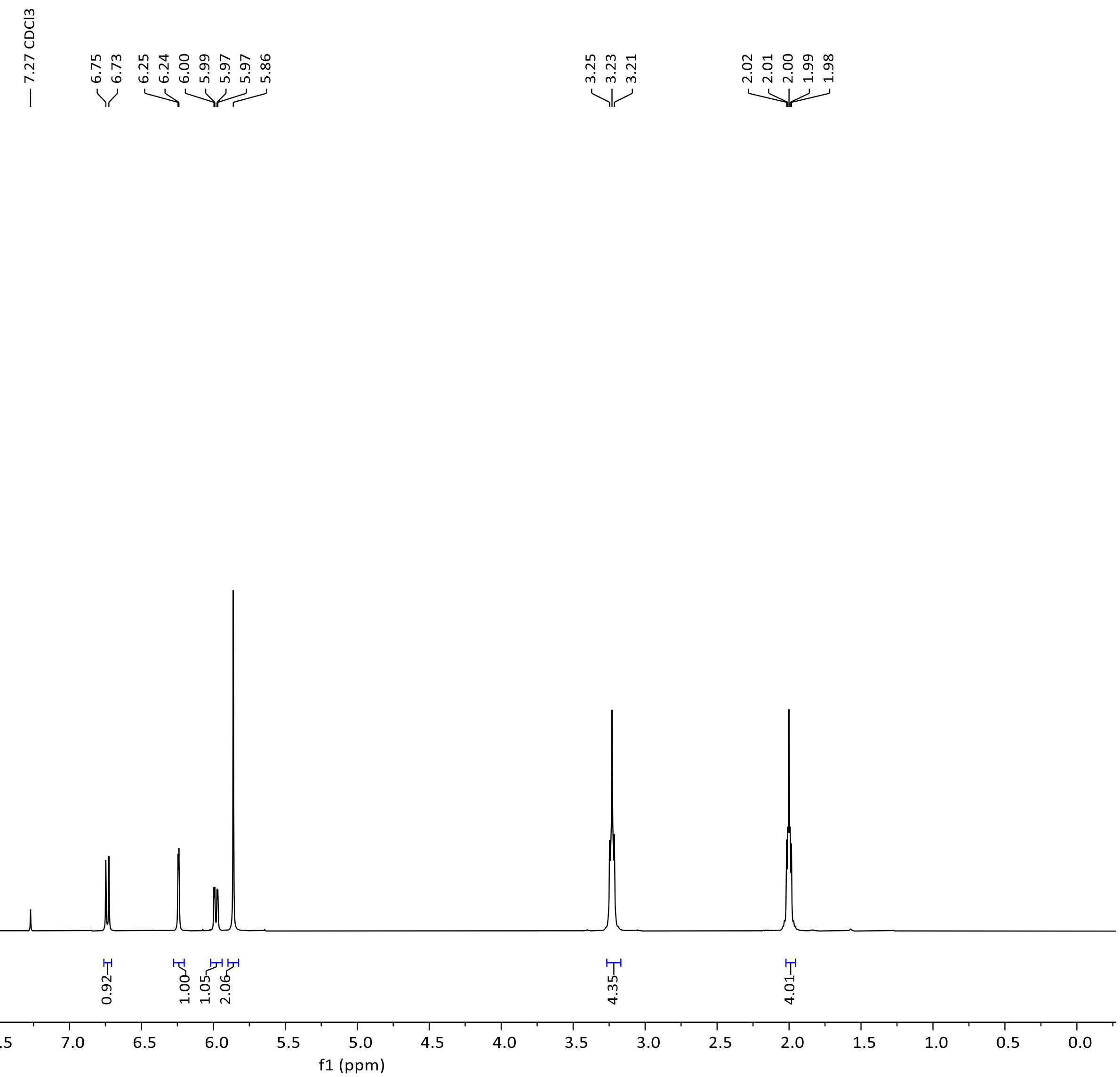


^{1}H NMR spectrum of **17** (600 MHz, $CDCl_3$)

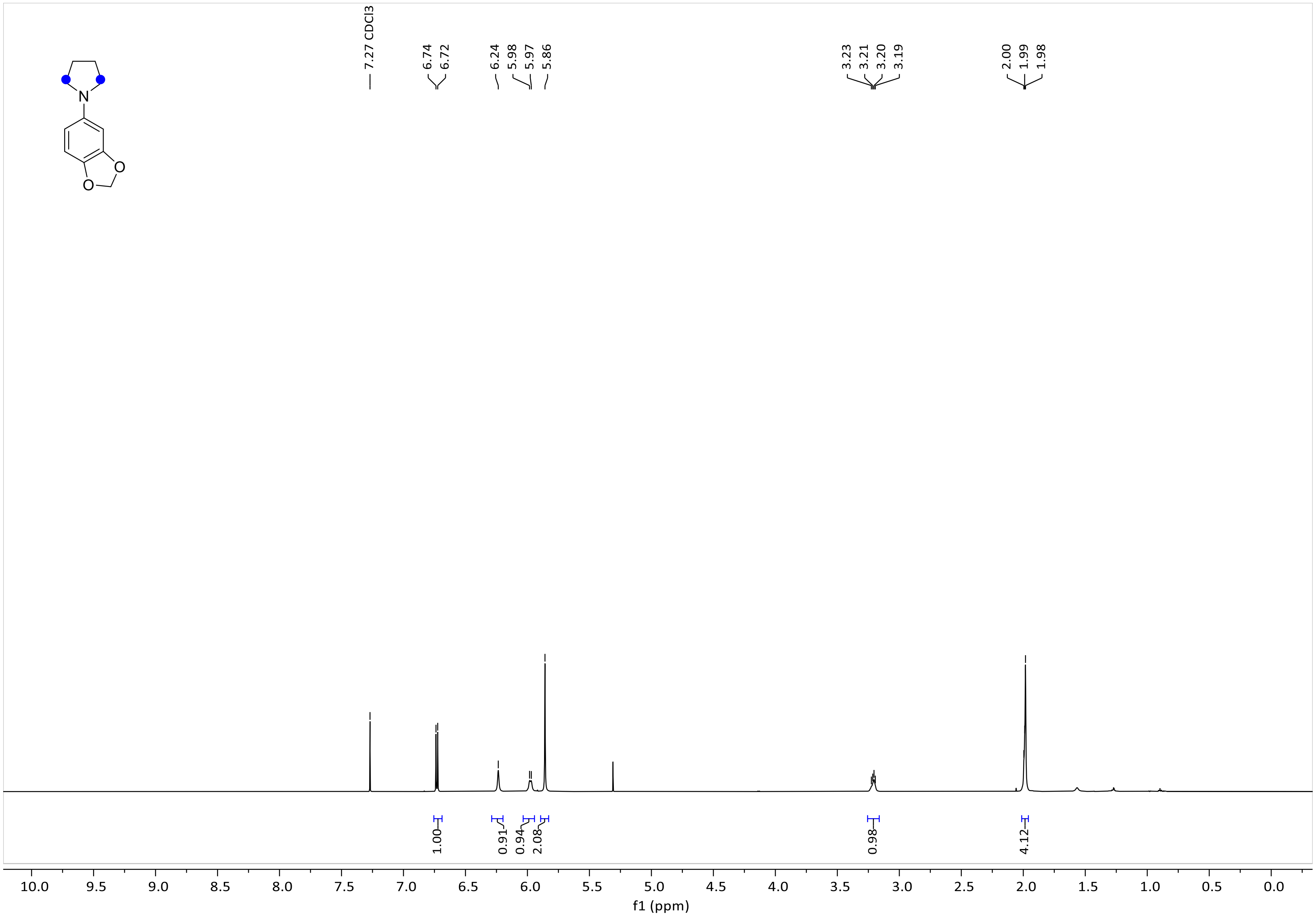


^{1}H NMR spectrum of **17a** (600 MHz, $CDCl_3$)

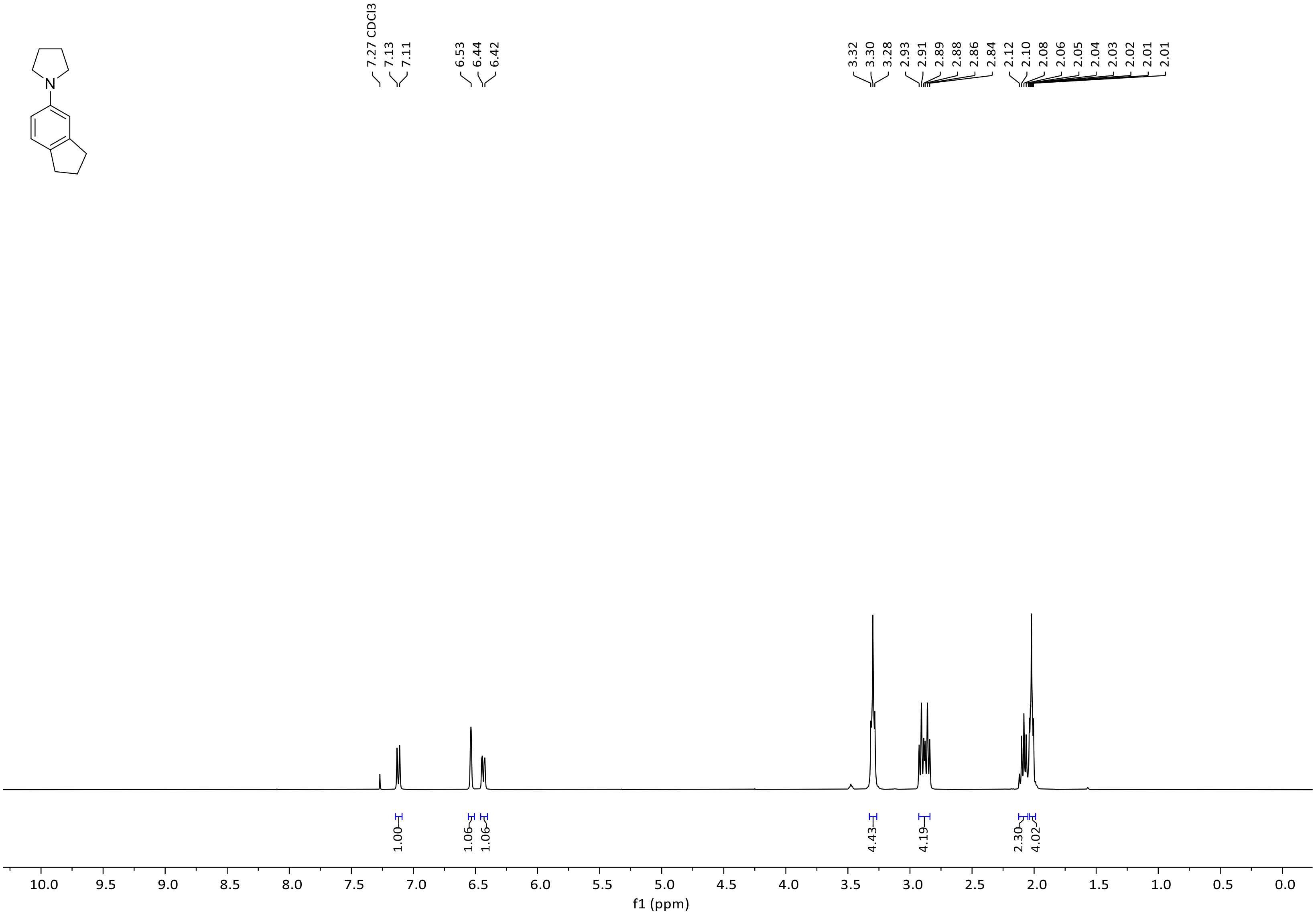




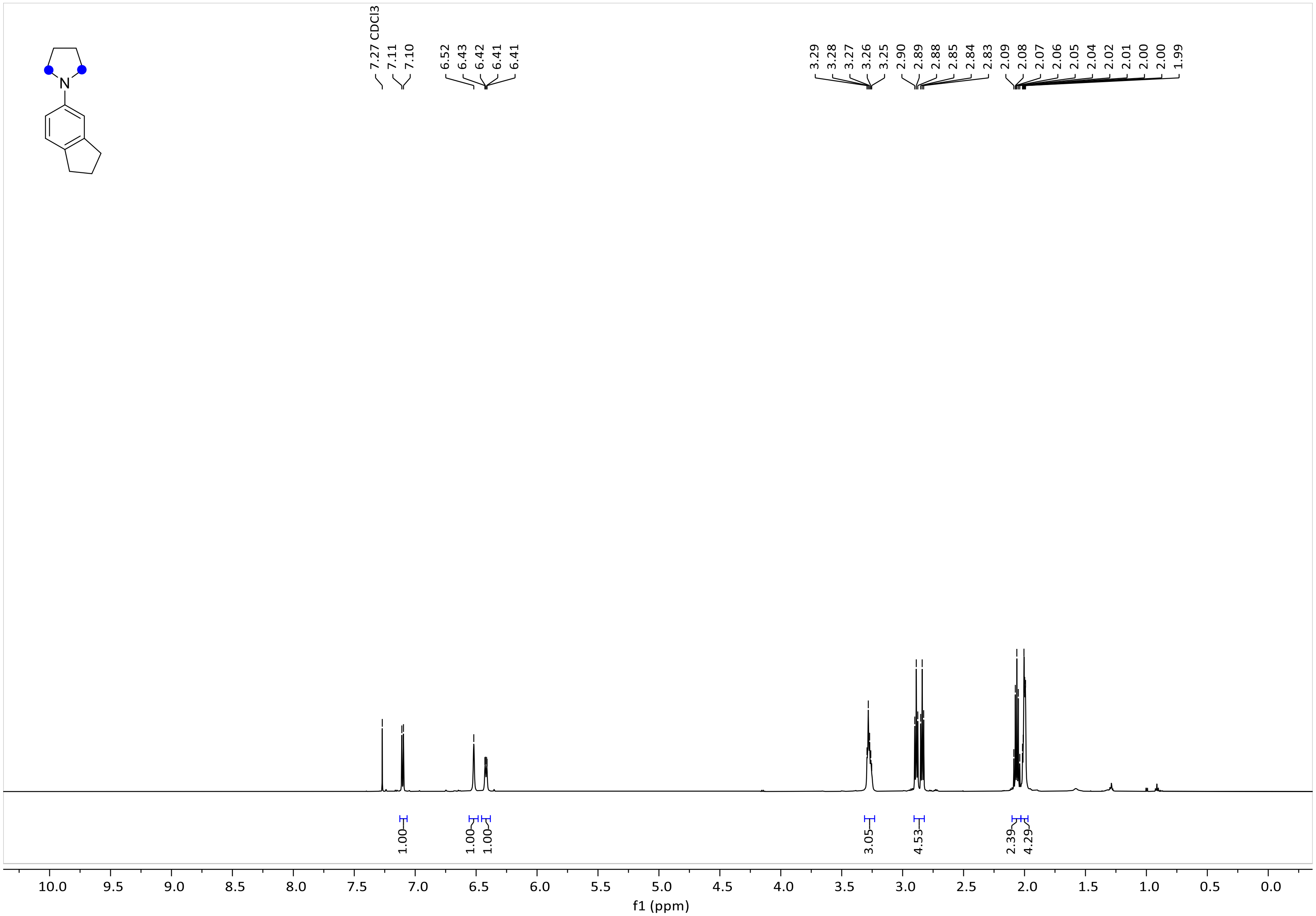
[1]H NMR spectrum of **18** (600 MHz, $CDCl_3$)



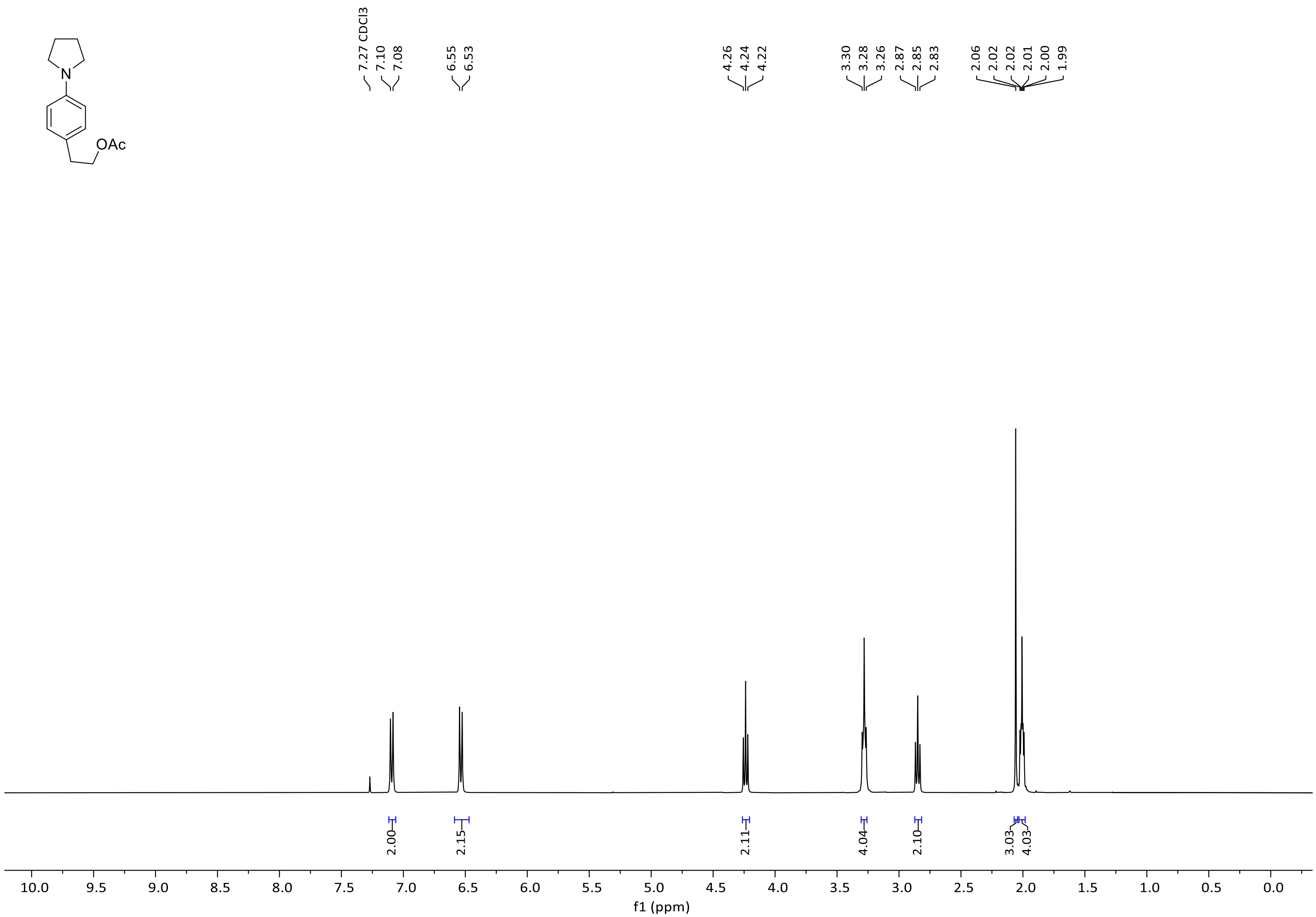
^{1}H NMR spectrum of **18a** (600 MHz, $CDCl_3$)



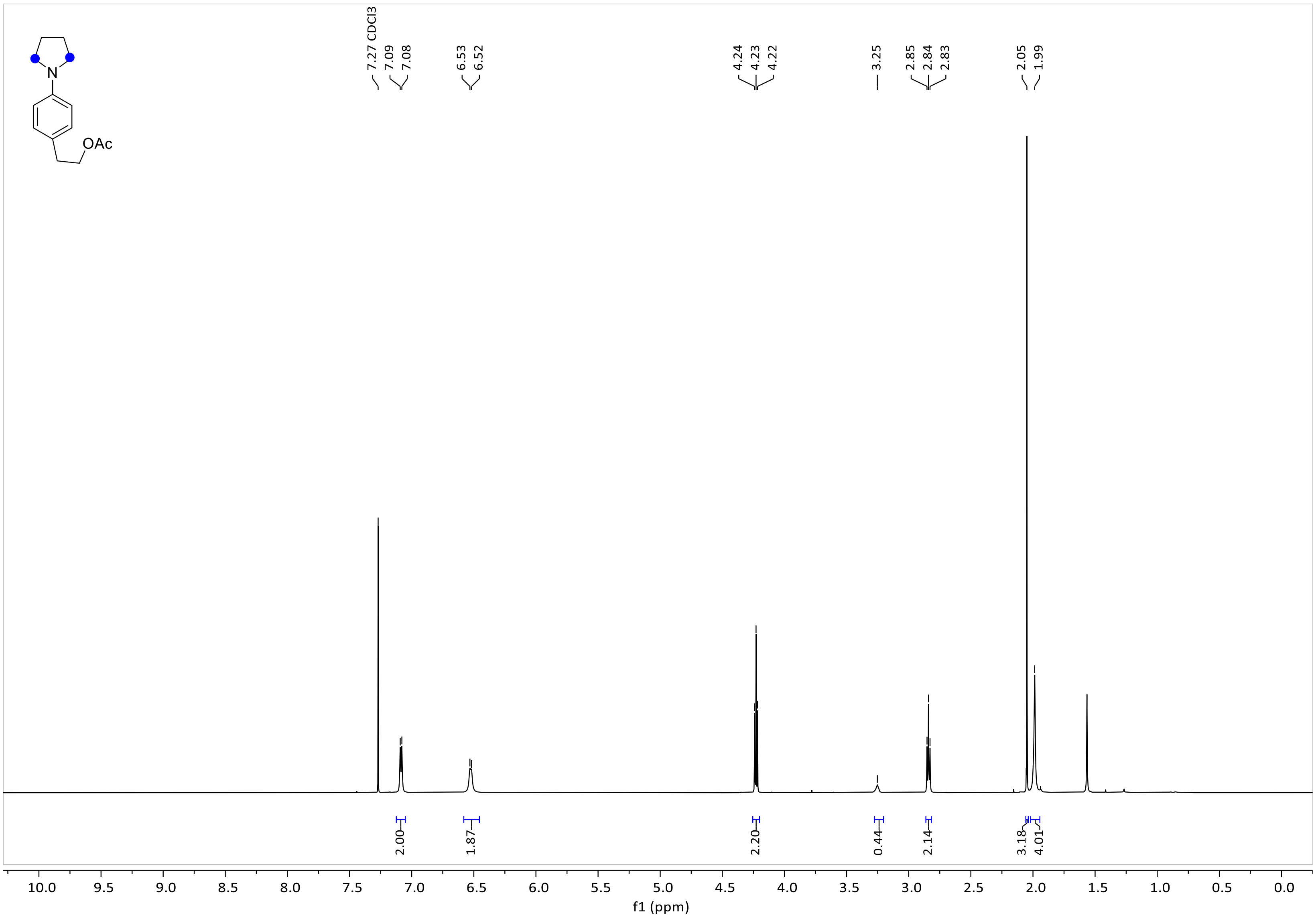
[1]H NMR spectrum of **19** (600 MHz, $CDCl_3$)



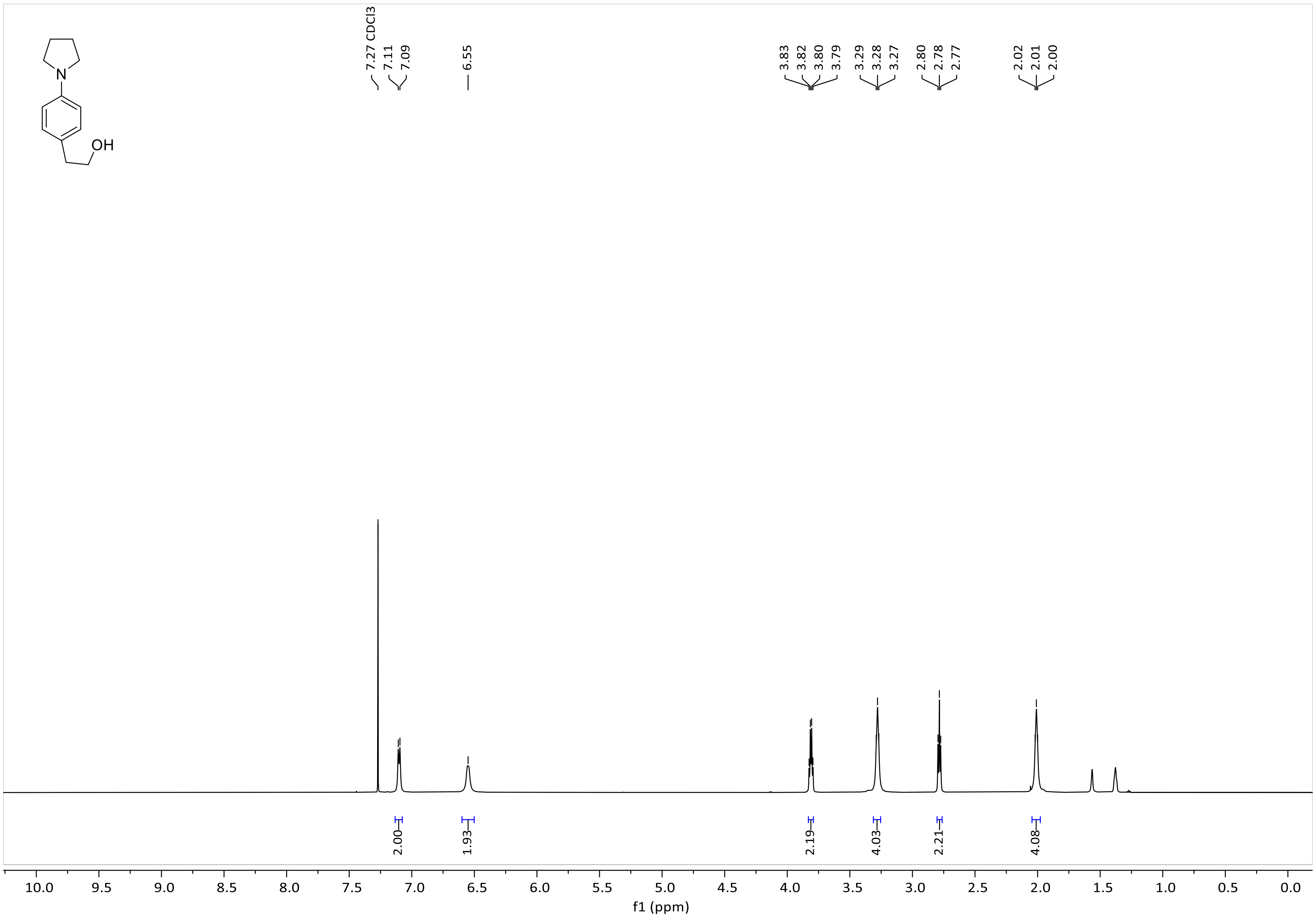
^{1}H NMR spectrum of **19a** (600 MHz, $CDCl_3$)



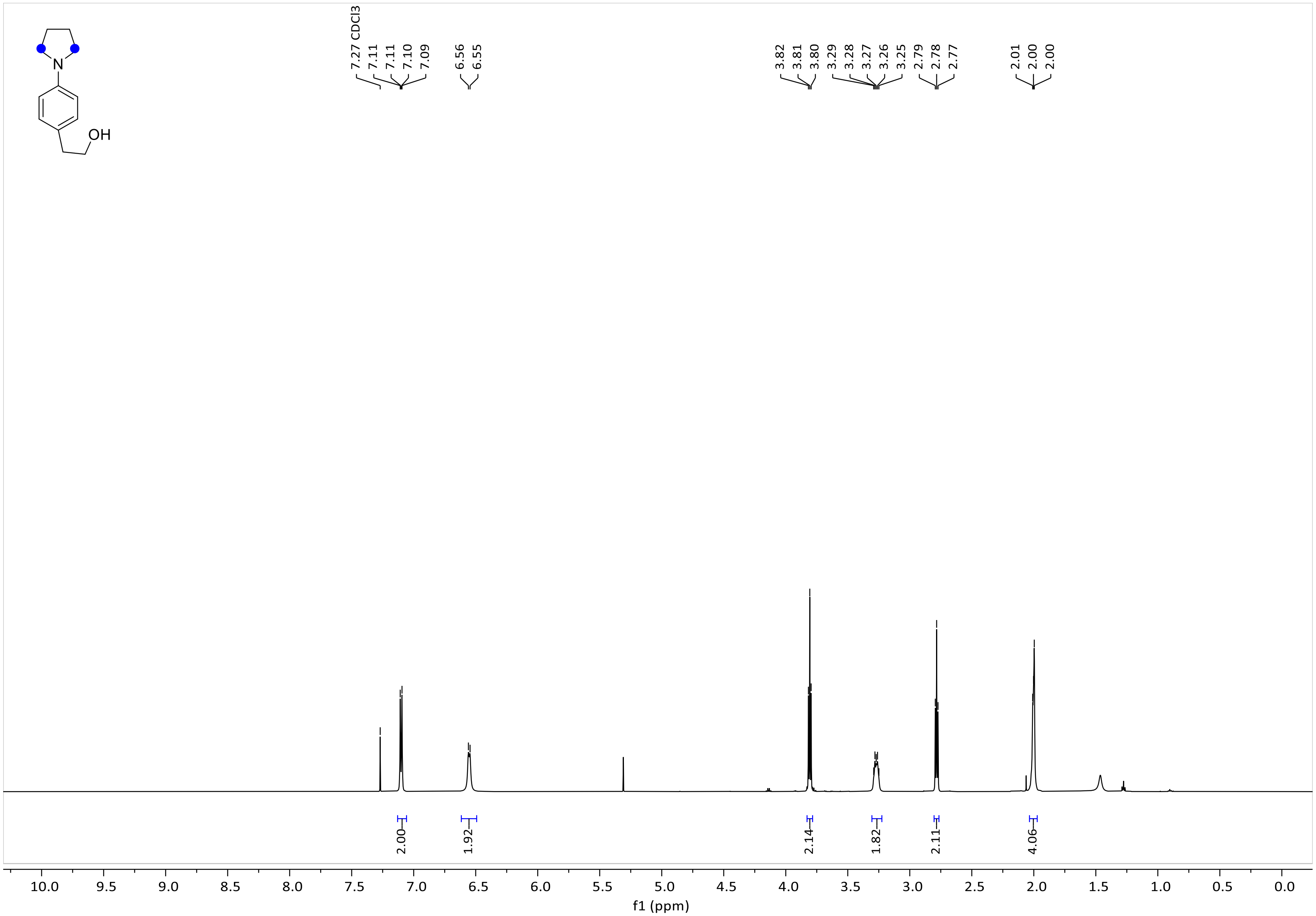
^{1}H NMR spectrum of **20** (600 MHz, $CDCl_3$)



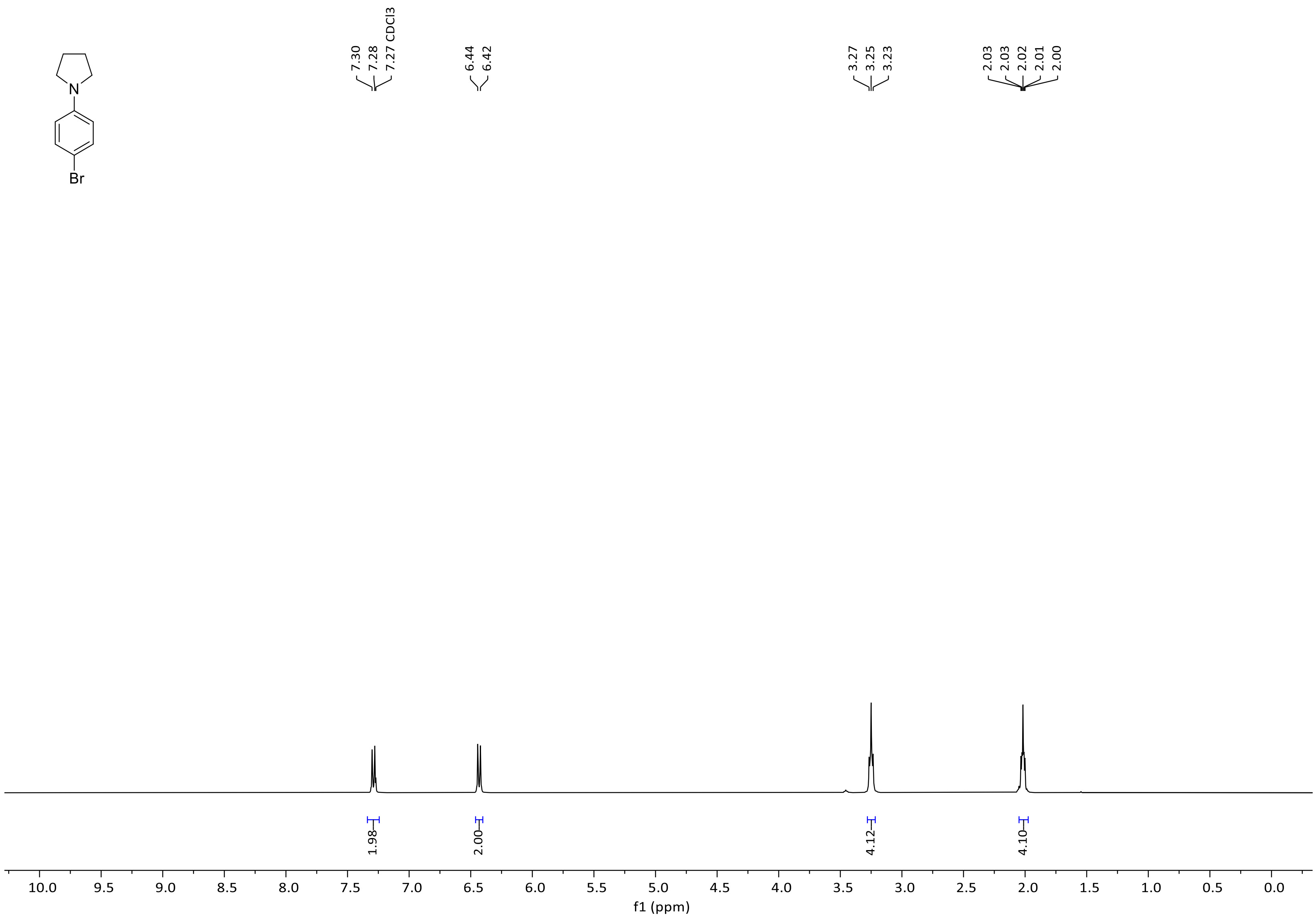
^{1}H NMR spectrum of **20a** (600 MHz, $CDCl_3$)



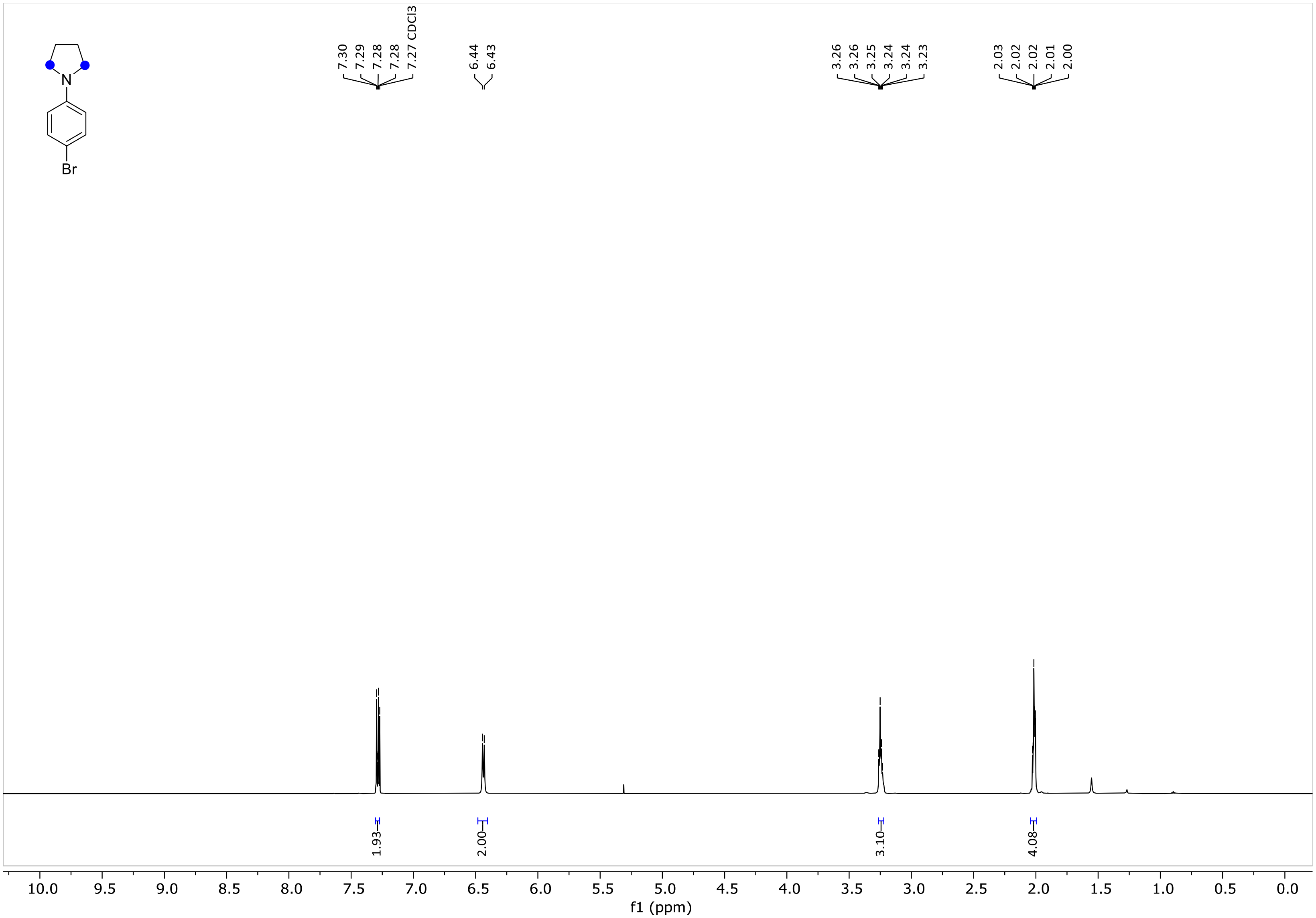
^{1}H NMR spectrum of **21** (600 MHz, $CDCl_3$)



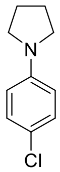
^{1}H NMR spectrum of **21a** (600 MHz, $CDCl_3$)

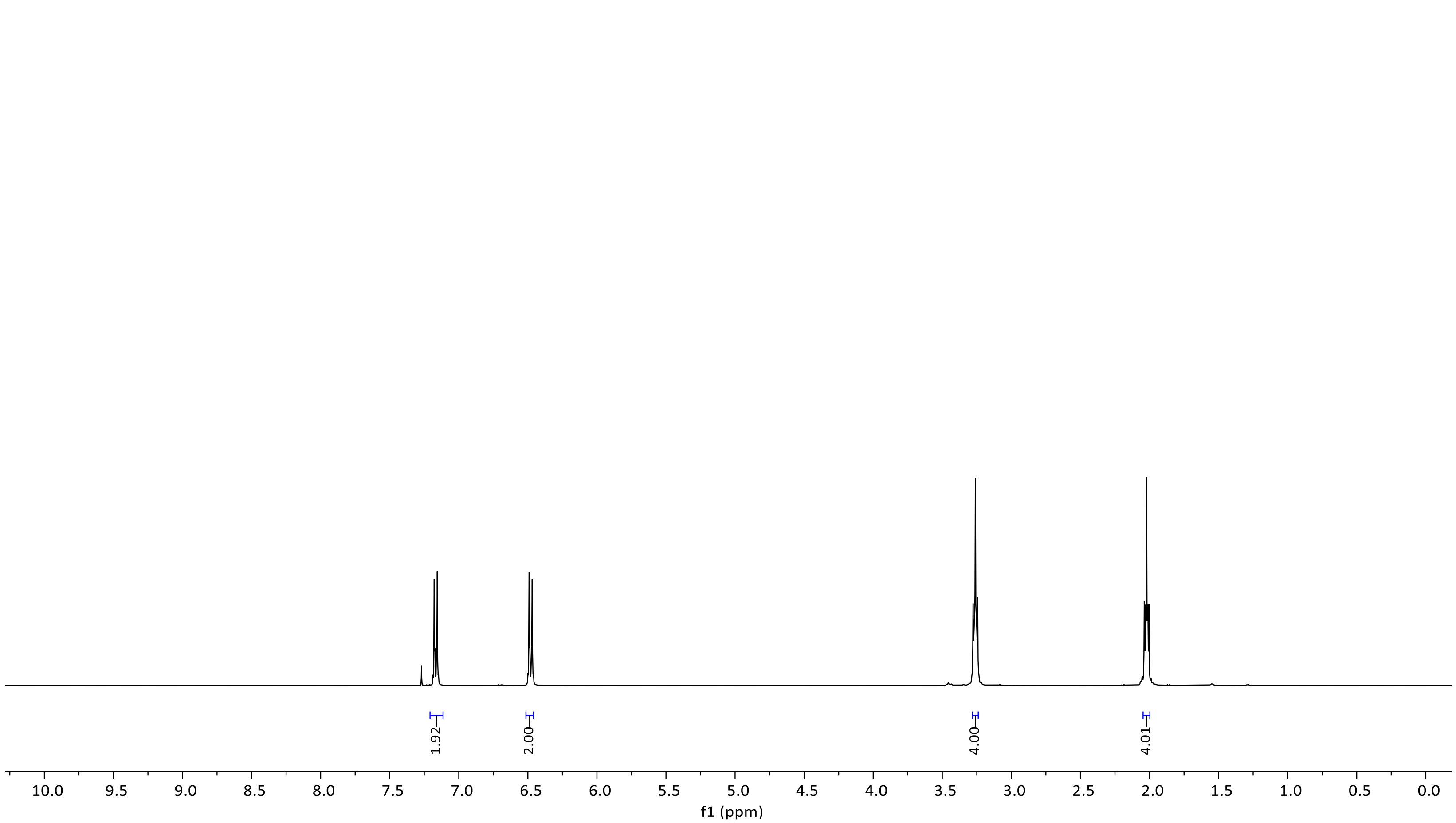


^{1}H NMR spectrum of **22** (600 MHz, $CDCl_3$)

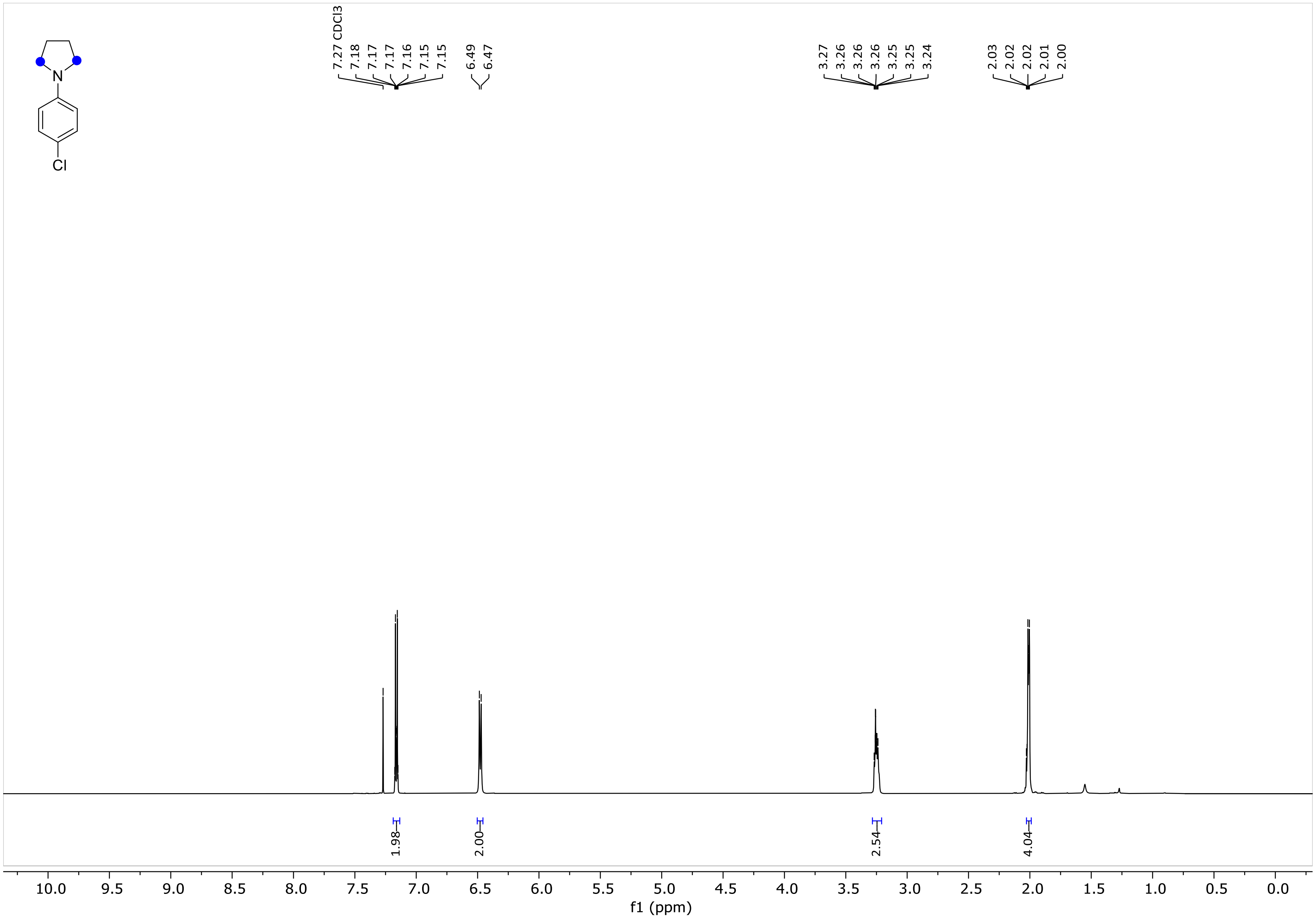


^{1}H NMR spectrum of **22a** (600 MHz, $CDCl_3$)

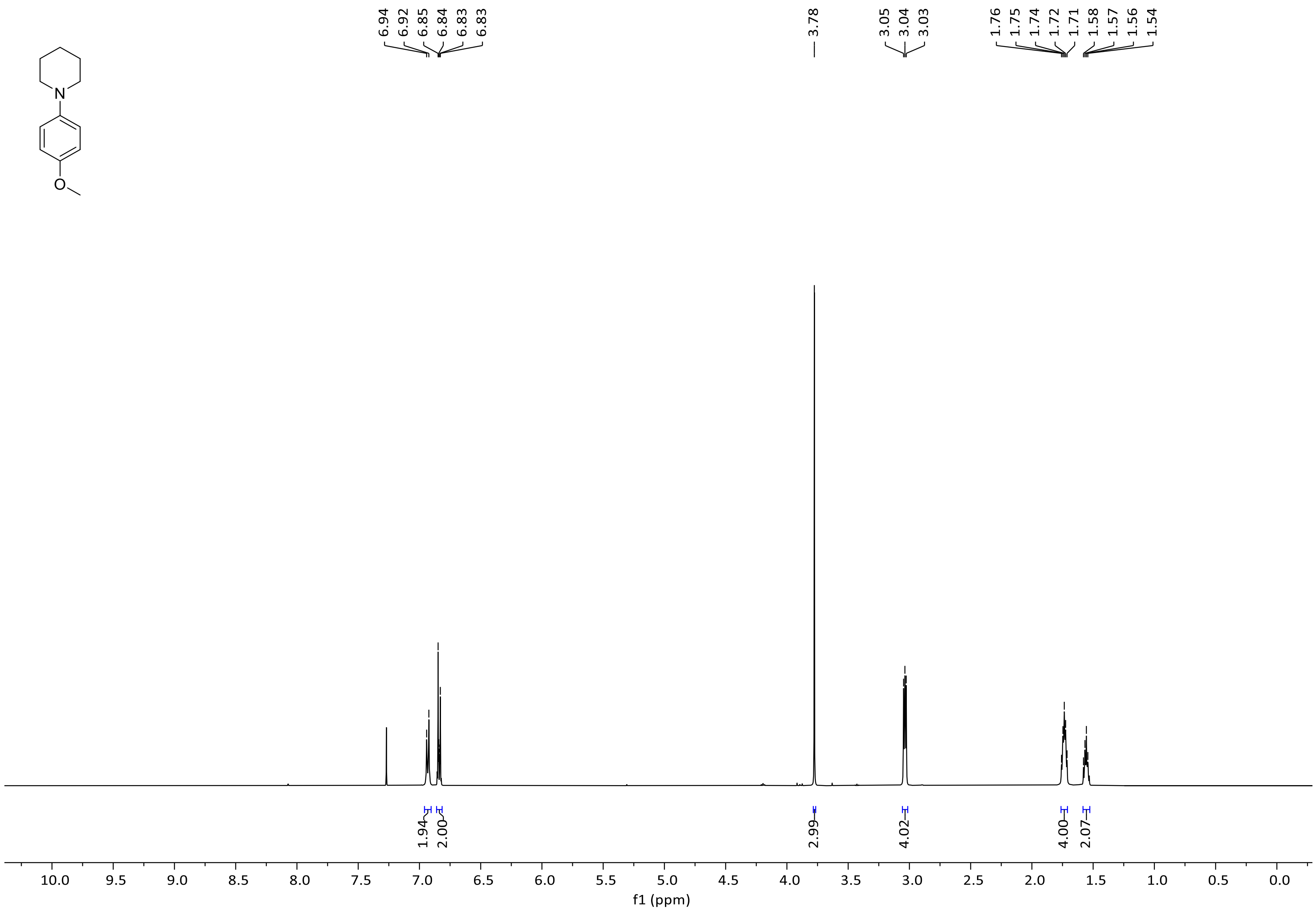




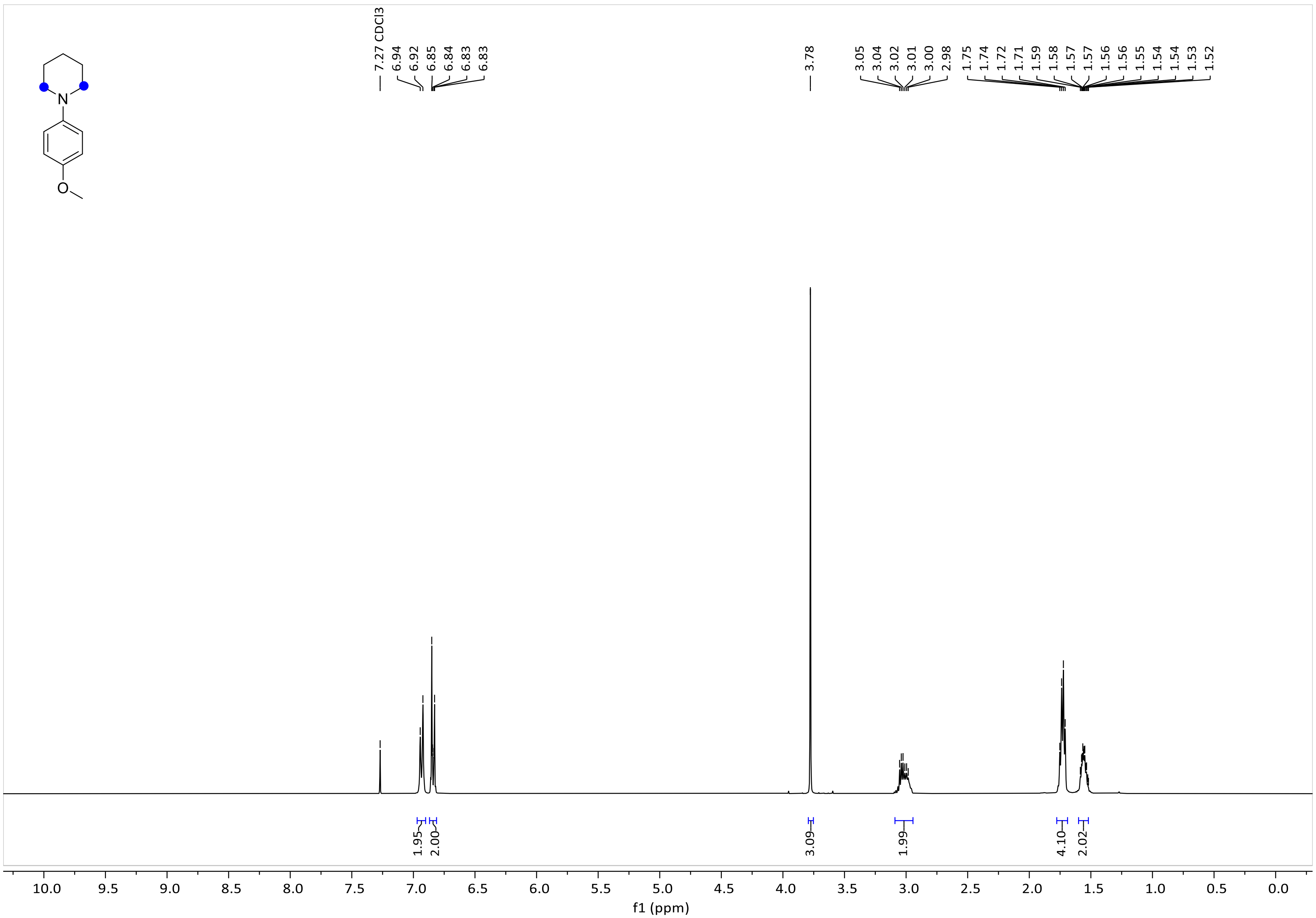
^{1}H NMR spectrum of **23** (600 MHz, $CDCl_3$)



^{1}H NMR spectrum of **23a** (600 MHz, $CDCl_3$)

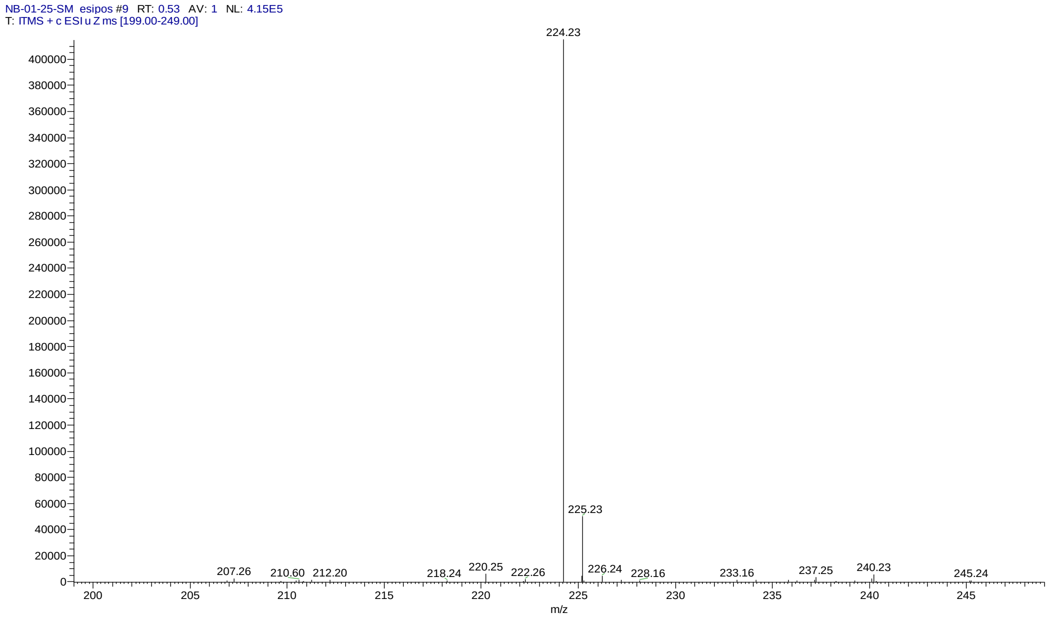


[1]H NMR spectrum of **24** (600 MHz, $CDCl_3$)

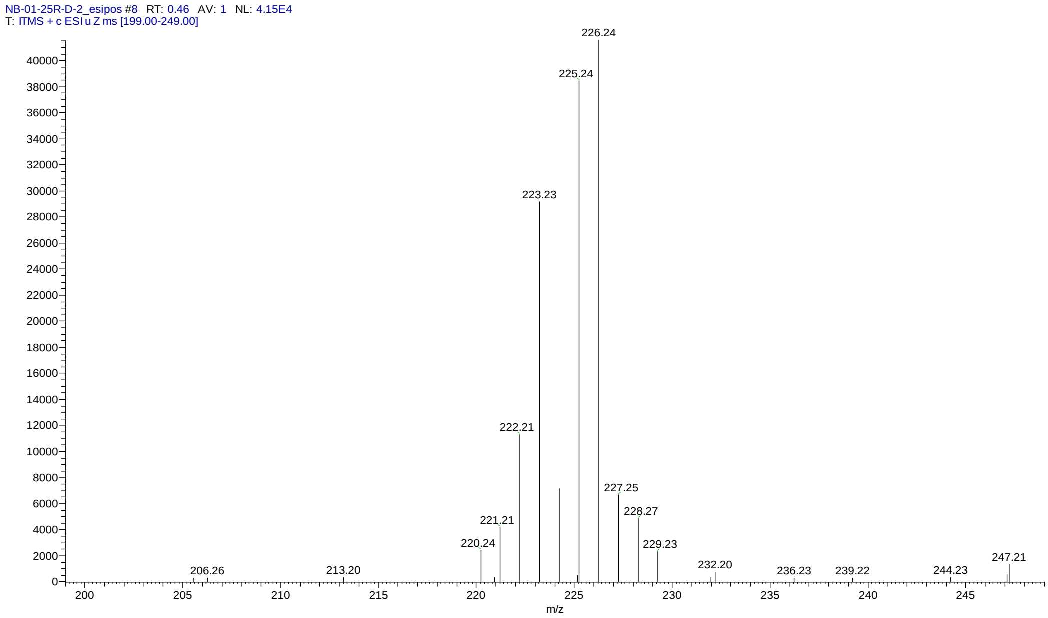


^{1}H NMR spectrum of **24a** (600 MHz, $CDCl_3$)

Appendix B. Copies of LC-MS raw data and fitting results



Mass spectrum of **1**.

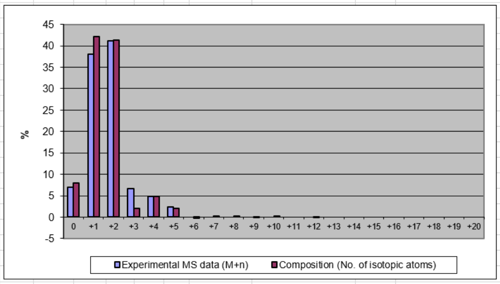


Mass spectrum of **1a**.

Unlabeled compound		Analyte
	Abundance	Abundance
M+1 462	414667.75	7118.1104
M+2	49914.055	38450.609
M+3	4448.3926	41548.57
M+4	0	6699.1338
M+5	0	4881.6157
M+6	0	2319.845
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

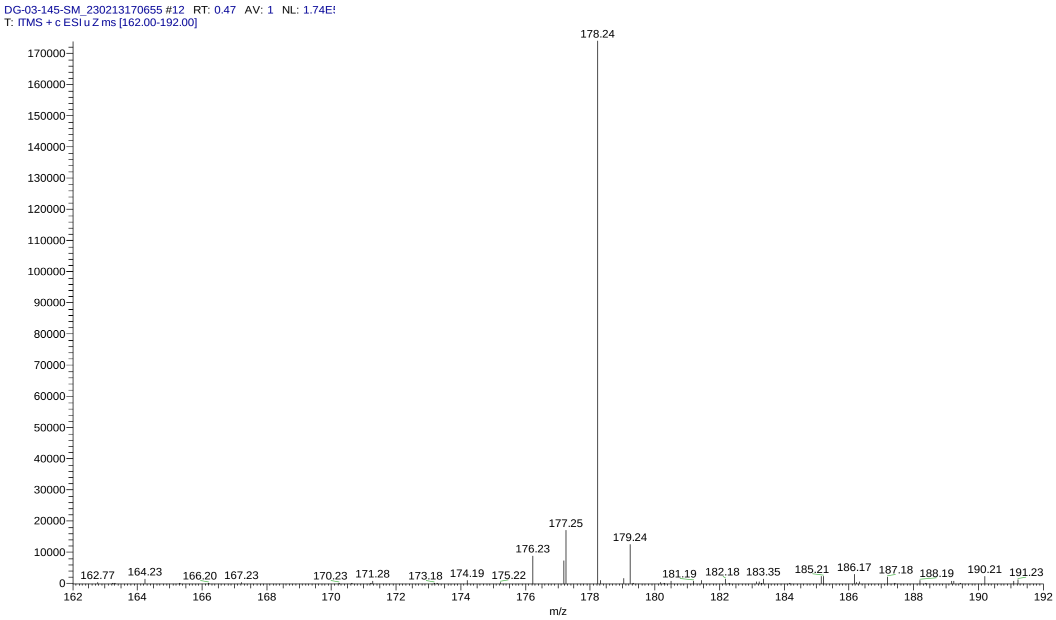
Expected derivatives: 14 | Labelled atoms 13 | Atom% 12.2

Calculate

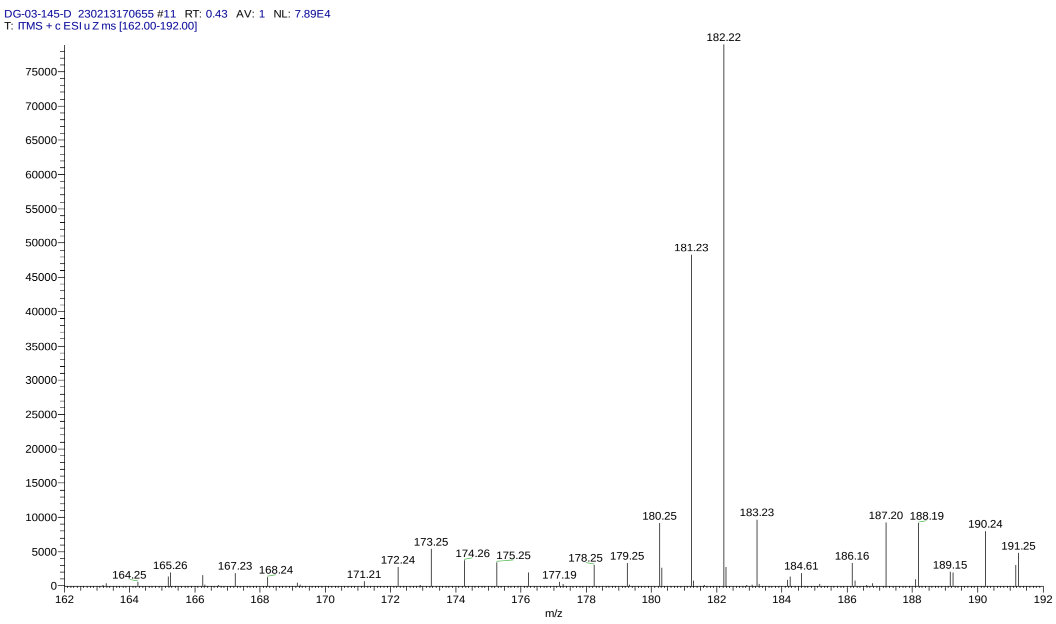


Results			
Relative amounts [%]			
unlabeled	8.0		
1-label	42.1	1	42.1
2-label	41.4	2	82.7
3-label	2.1	3	6.21
4-label	4.8	4	19.1
5-label	2.0	5	10
6-label	-0.3	6	-1.8
7-label	0.0	7	0.1
8-label	0.0	8	0.01
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	0
12-label	0.0	12	-0
13-label	0.0	13	0
		Total:	1.58

Mass spectrum and isopat analysis of **1a**.



Mass spectrum of **2**.



Mass spectrum of **2a**.

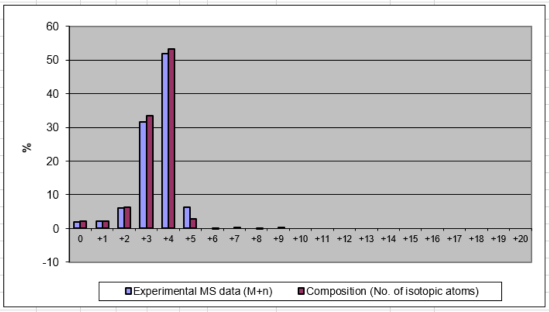
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	173904.66	3015.7654
M+2	12474.899	3295.7217
M+3	0	9076.8809
M+4	0	48276.836
M+5	0	78890.586
M+6	0	9617.4648
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14

Calculate

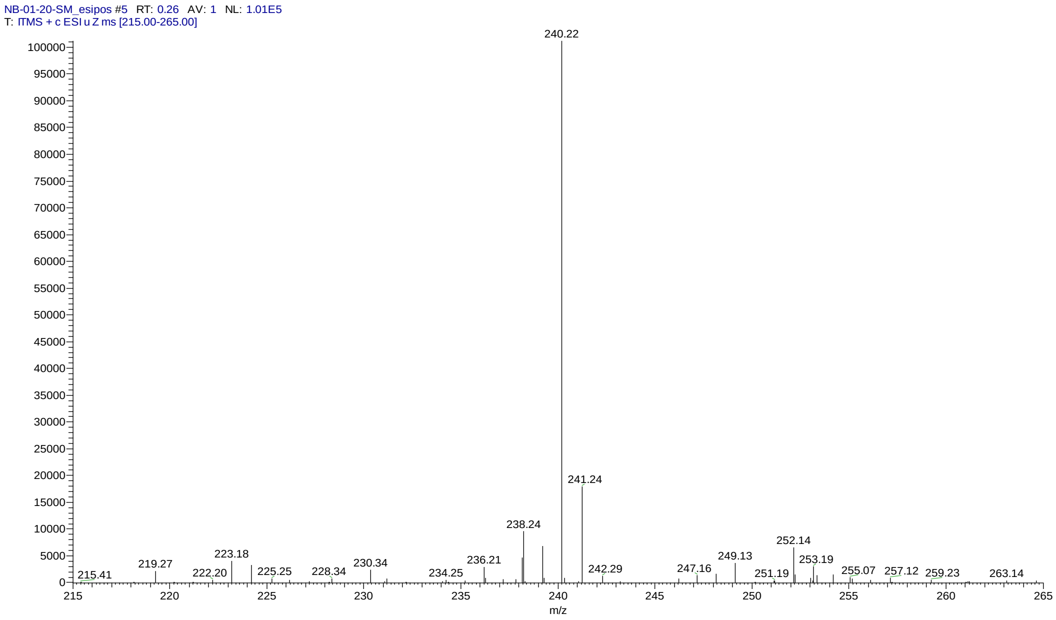
Labelled atoms 13

Atom% 26.3

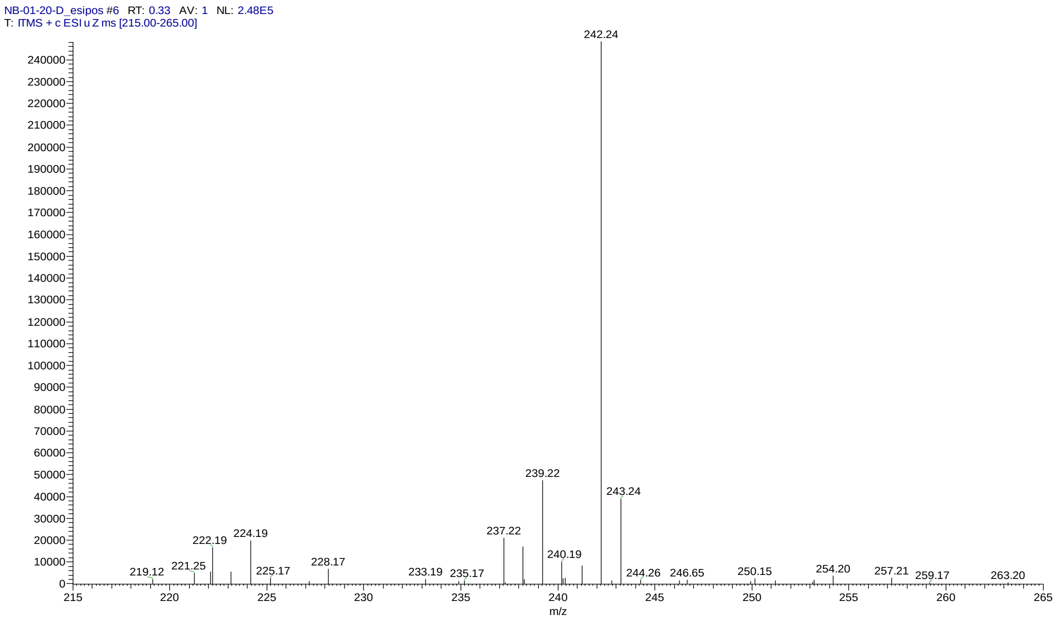


Results Relative amounts [%]			
unlabeled	2.1		
1-label	2.2	1	2.17
2-label	6.2	2	12.5
3-label	33.6	3	101
4-label	53.2	4	213
5-label	3.0	5	14.8
6-label	-0.2	6	-1.3
7-label	0.0	7	0.11
8-label	0.0	8	-0
9-label	0.0	9	0
10-label	0.0	10	-0
11-label	0.0	11	0
12-label	0.0	12	-0
13-label	0.0	13	0
		Total:	3.42

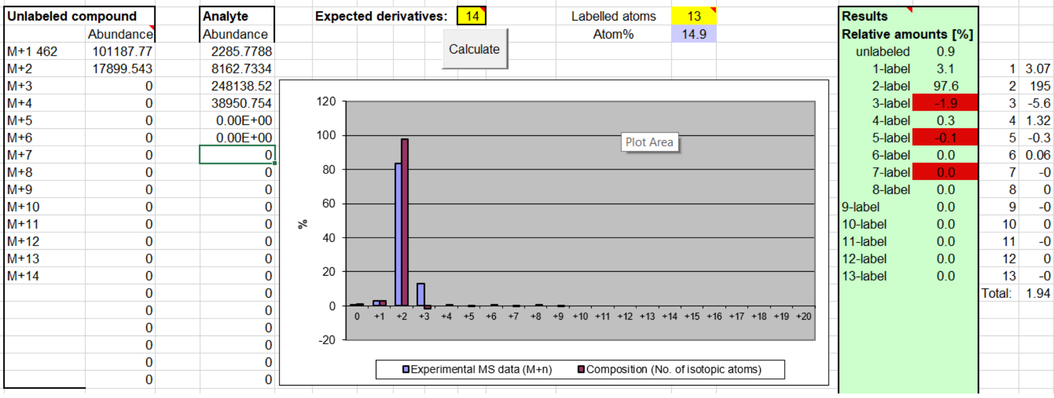
Mass spectrum and isopat analysis of **2a**.



Mass spectrum of **3**.



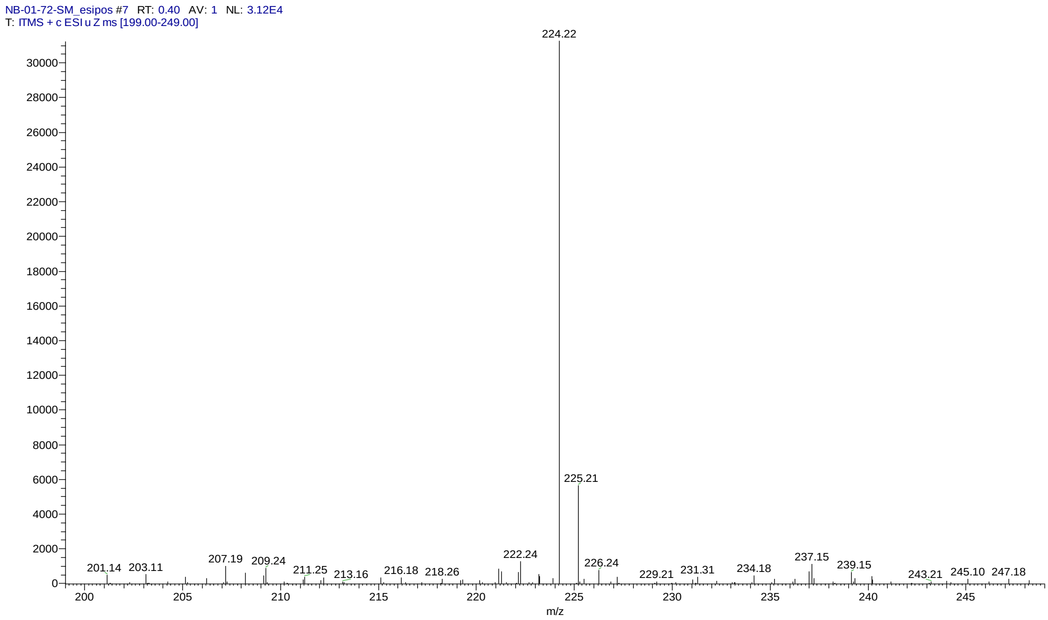
Mass spectrum of **3a**.



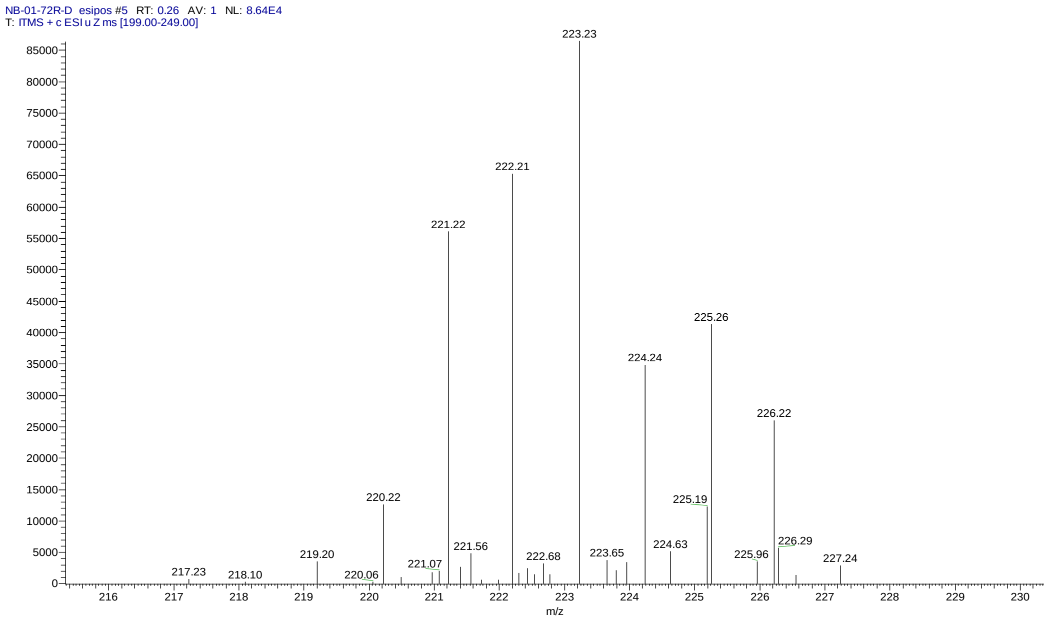
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	101187.77	2285.7788
M+2	17899.543	8162.7334
M+3	0	248138.52
M+4	0	38950.754
M+5	0	0.00E+00
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Results Relative amounts [%]			
unlabeled	0.9		
1-label	3.1	1	3.07
2-label	97.6	2	195
3-label	-1.9	3	-5.6
4-label	0.3	4	1.32
5-label	-0.1	5	-0.3
6-label	0.0	6	0.06
7-label	0.0	7	-0
8-label	0.0	8	0
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	1.94

Mass spectrum and isopat analysis of **3a**.



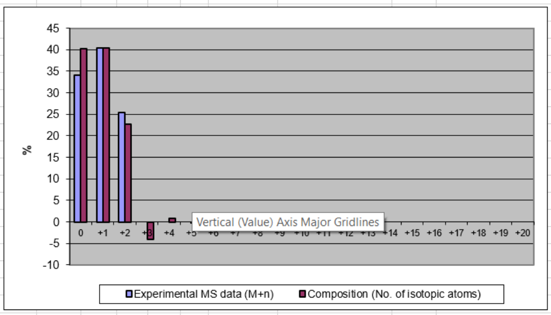
Mass spectrum of **4**.



Mass spectrum of **4a**.

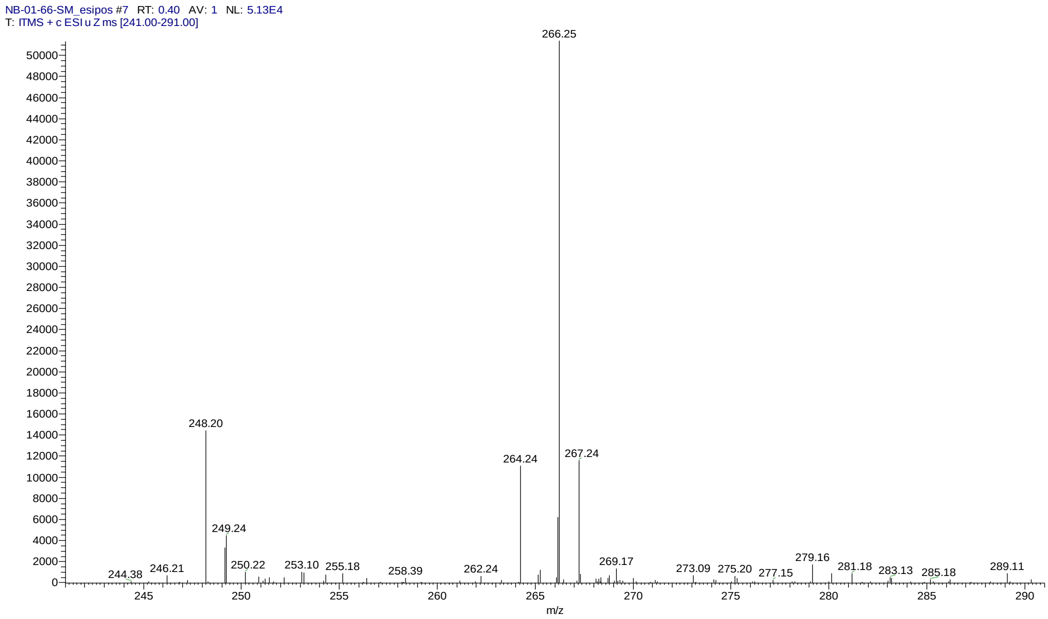
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	31237.91	34858.102
M+2	5636.894	41276.184
M+3	0	25977.543
M+4	0	0.00E+00
M+5	0	0.00E+00
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14 | Labelled atoms 13 | Atom% 5.8 | Calculate

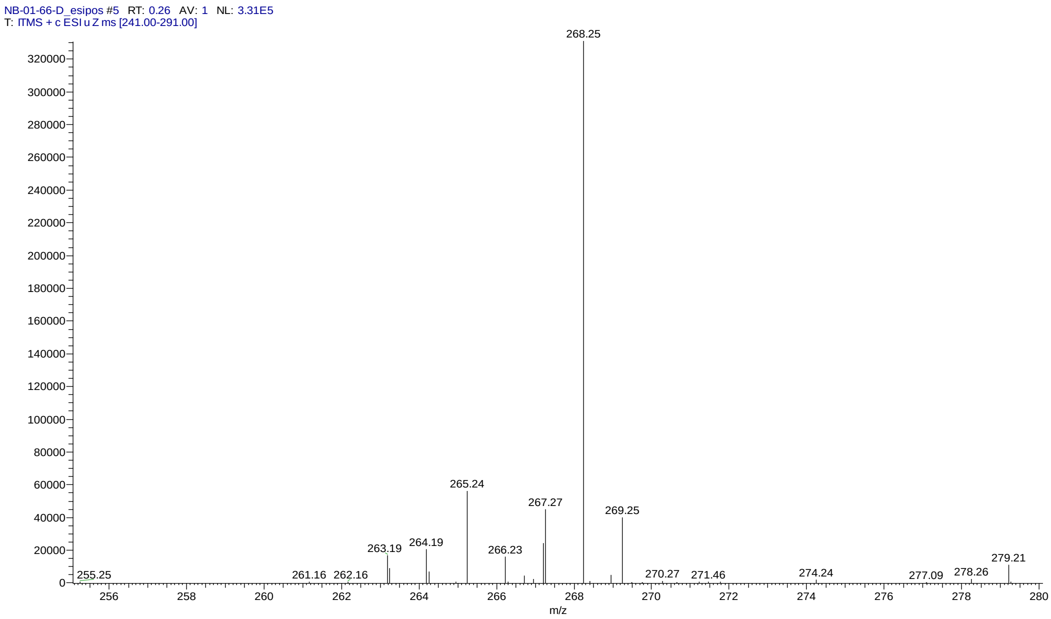


Results Relative amounts [%]			
unlabeled	40.3		
1-label	40.4	1	40.4
2-label	22.7	2	45.5
3-label	-4.1	3	-12
4-label	0.7	4	2.96
5-label	-0.1	5	-0.7
6-label	0.0	6	0.14
7-label	0.0	7	-0
8-label	0.0	8	0.01
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	0.76

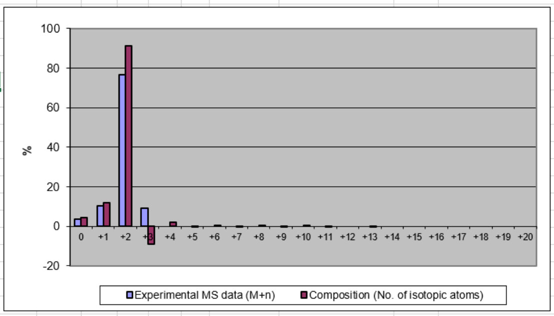
Mass spectrum and isopat analysis of **4a**.



Mass spectrum of **5**.



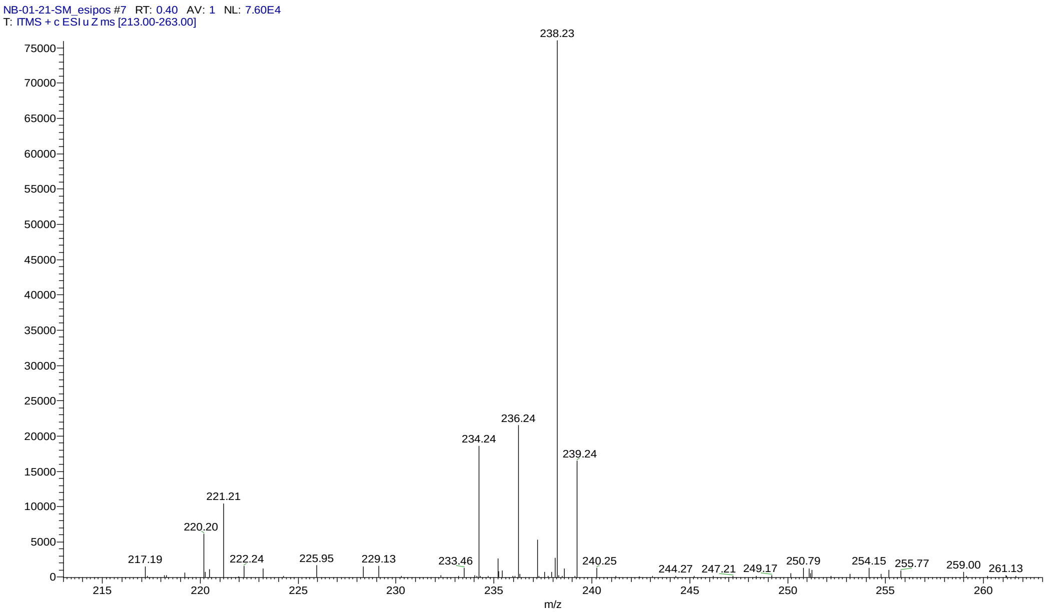
Mass spectrum of **5a**.



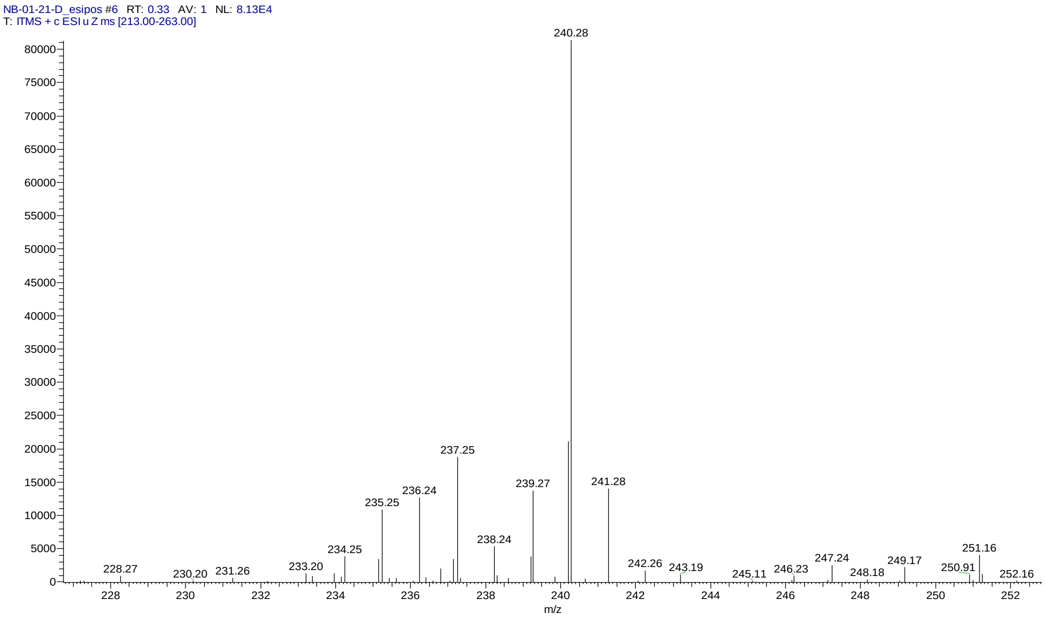
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	51326.34	16023.38
M+2	11553.463	45012.449
M+3	0	330667.19
M+4	0	40002.113
M+5	0	0.00E+00
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Results Relative amounts [%]			
unlabeled	4.5		
1-label	11.8	1	11.8
2-label	91.2	2	182
3-label	-9.2	3	-28
4-label	2.1	4	8.26
5-label	-0.5	5	-2.3
6-label	0.1	6	0.63
7-label	0.0	7	-0.2
8-label	0.0	8	0.04
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	1.73

Mass spectrum and isopat analysis of **5a**.



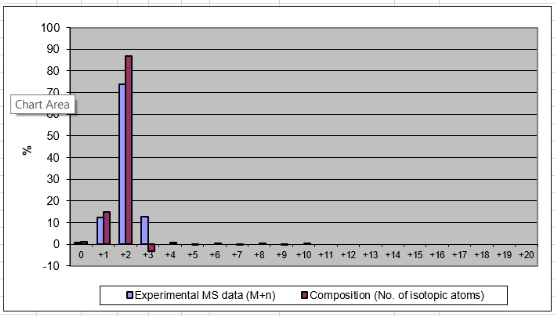
Mass spectrum of **6**.



Mass spectrum of **6a**.

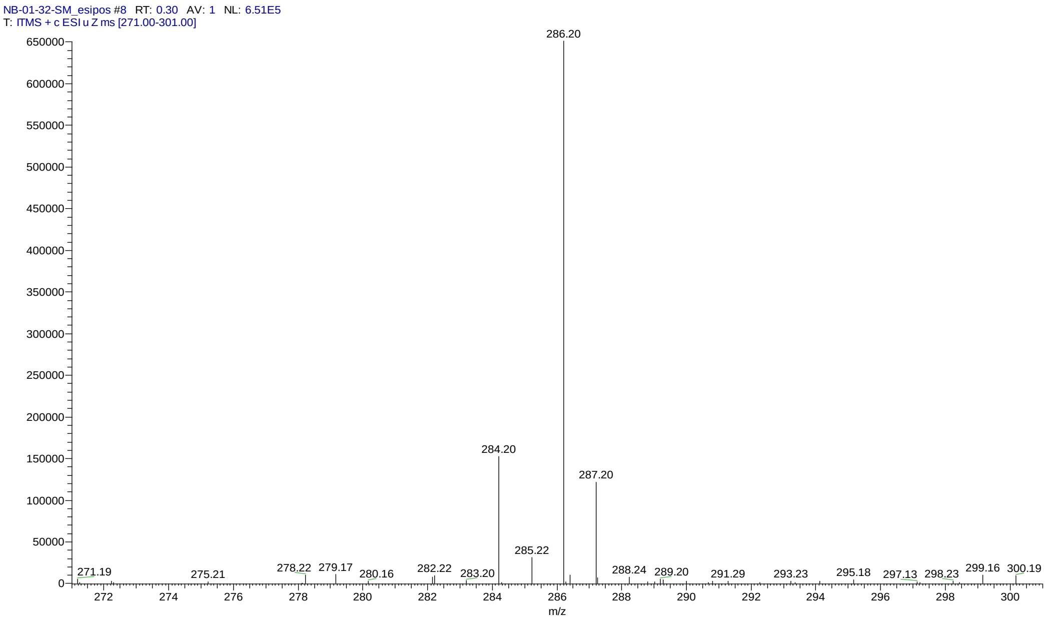
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	75952.078	924.87494
M+2	16449.814	13690.909
M+3	0	81278.492
M+4	0	13999.94
M+5	0	0.00E+00
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14 Labelled atoms 13 Atom% 13.9 Calculate

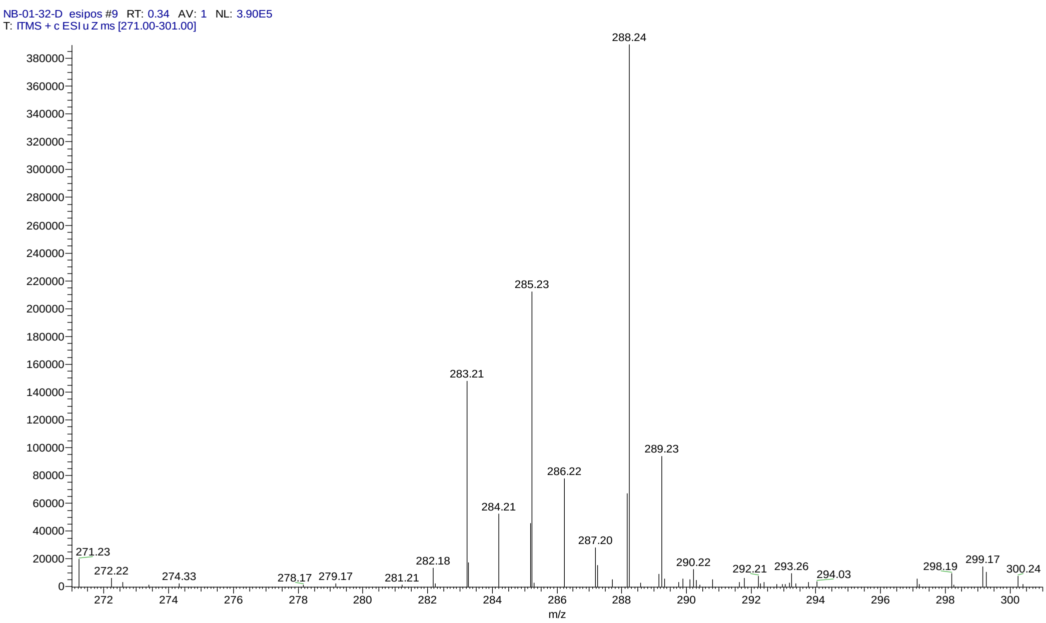


Results Relative amounts [%]			
unlabeled	1.0		
1-label	14.9	1	14.9
2-label	86.7	2	173
3-label	-3.3	3	-9.9
4-label	0.7	4	2.85
5-label	-0.2	5	-0.8
6-label	0.0	6	0.2
7-label	0.0	7	-0.1
8-label	0.0	8	0.01
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	1.81

Mass spectrum and isopat analysis of **6a**.



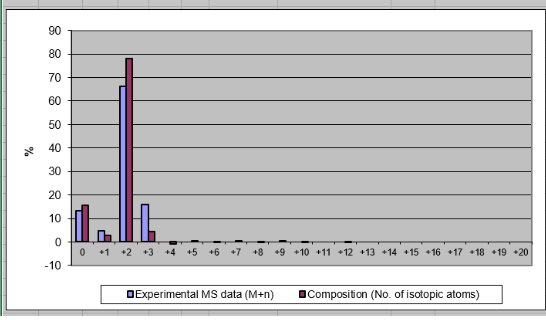
Mass spectrum of **7**.



Mass spectrum of **7a**.

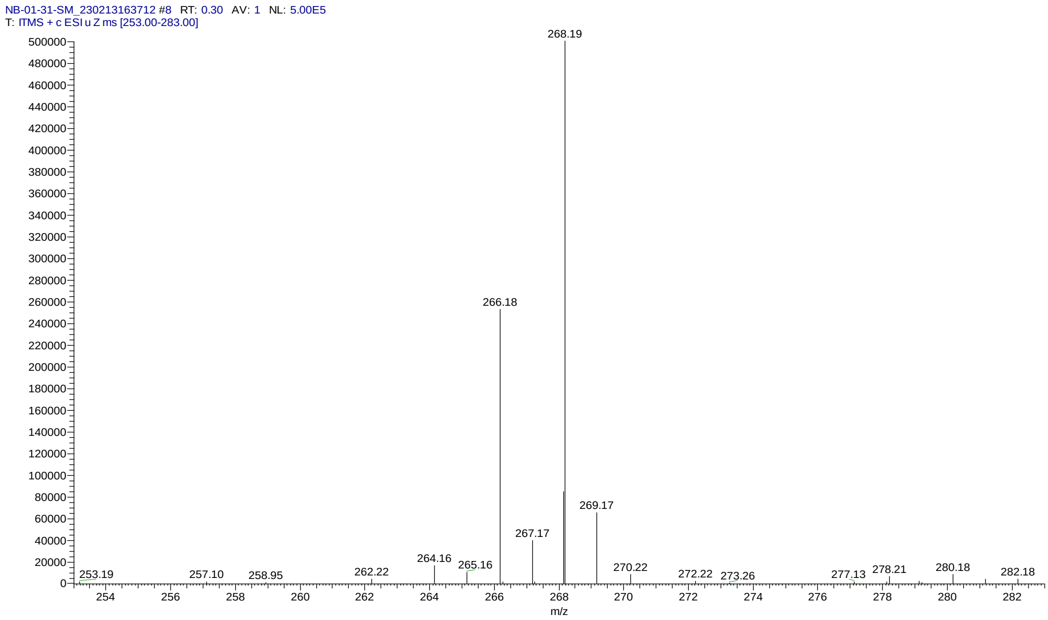
Unlabeled compound		Analyte
	Abundance	Abundance
M+1 462	650810.25	77643.758
M+2	121237.12	27787.521
M+3	0	389532.38
M+4	0	93731.133
M+5	0	0.00E+00
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14 | Labelled atoms 13 | Atom% 13.0 | Calculate

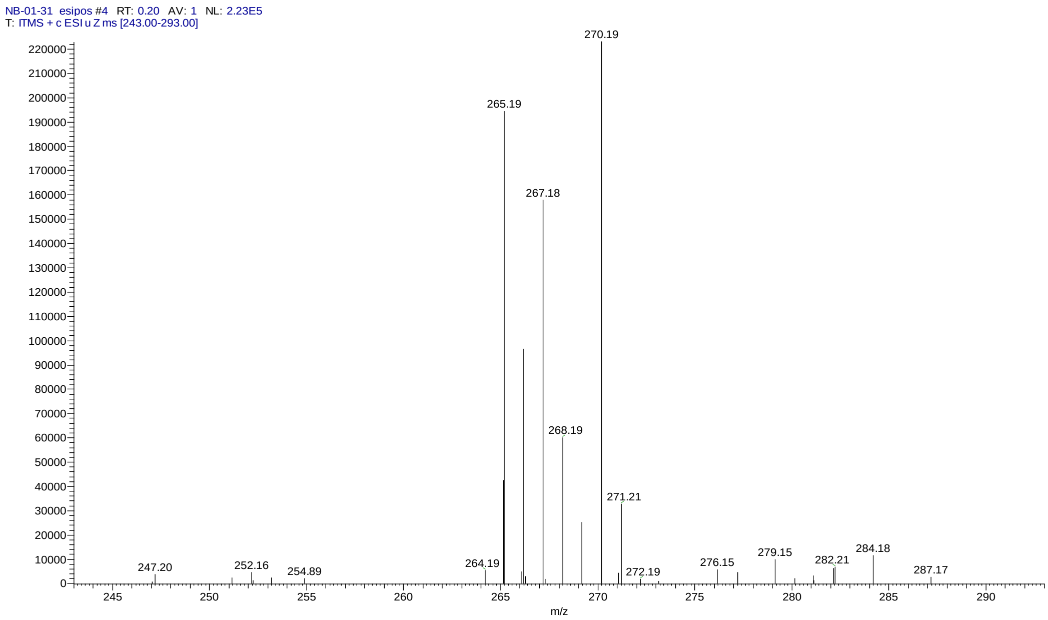


Results			
Relative amounts [%]			
unlabeled	15.6		
1-label	2.7	1	2.68
2-label	78.0	2	156
3-label	4.4	3	13.1
4-label	-0.8	4	-3.2
5-label	0.2	5	0.76
6-label	0.0	6	-0.2
7-label	0.0	7	0.04
8-label	0.0	8	-0
9-label	0.0	9	0
10-label	0.0	10	-0
11-label	0.0	11	0
12-label	0.0	12	-0
13-label	0.0	13	0
		Total:	1.69

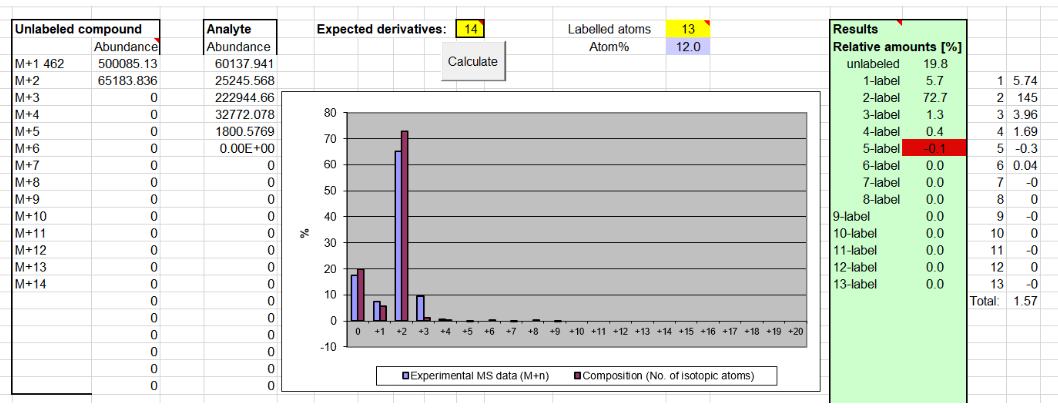
Mass spectrum and isopat analysis of **7a**.



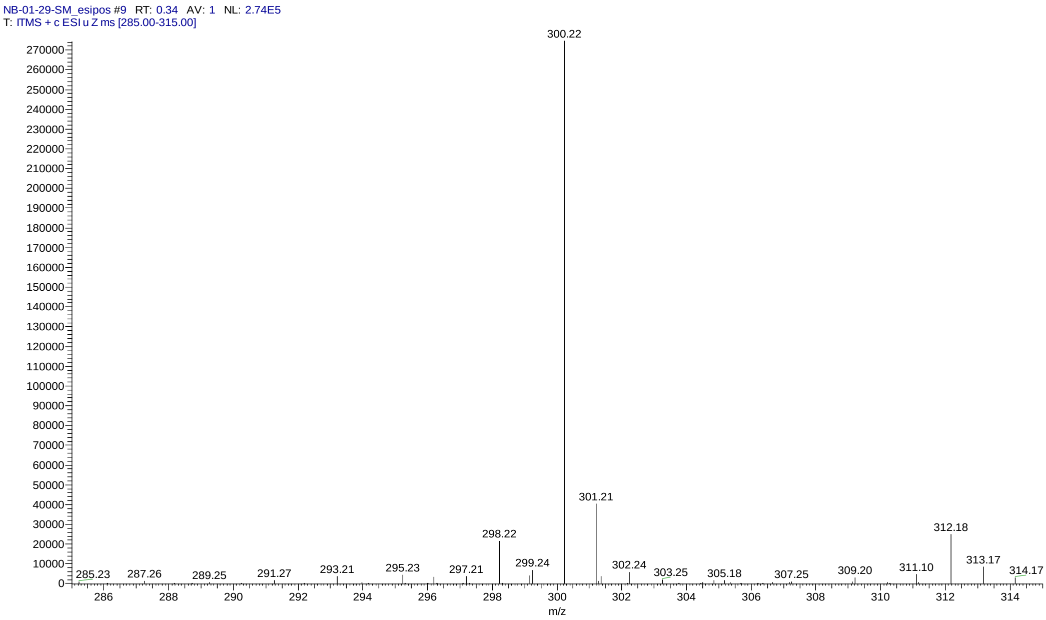
Mass spectrum of **8**.



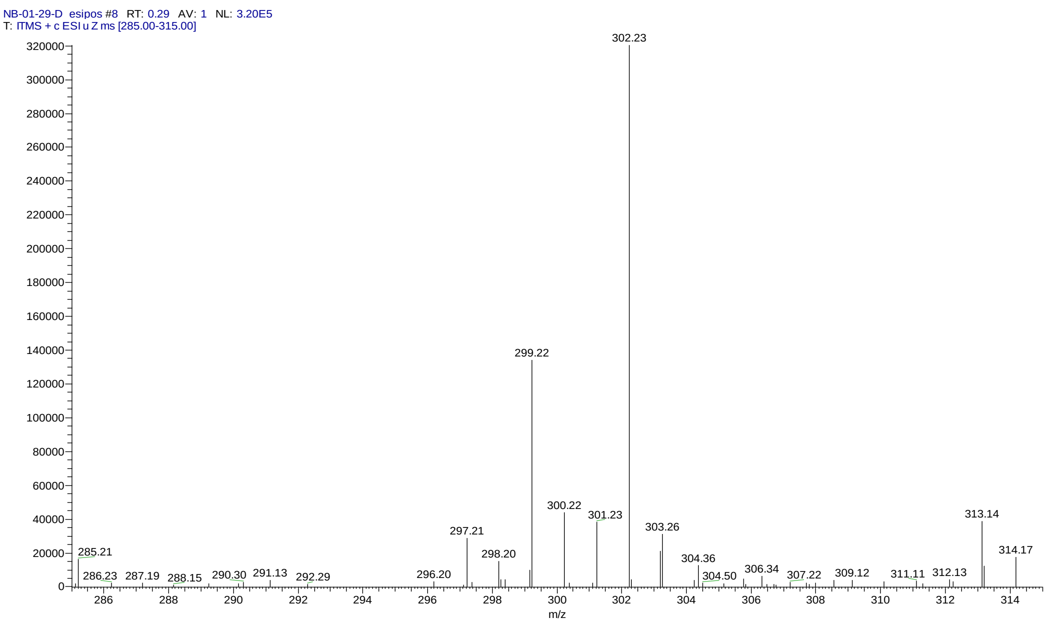
Mass spectrum of **8a**.



Mass spectrum and isopat analysis of **8a**.



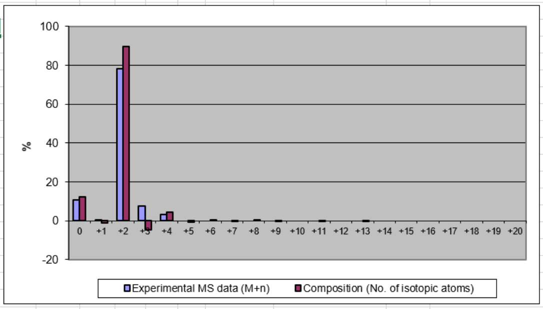
Mass spectrum of **9**.



Mass spectrum of **9a**.

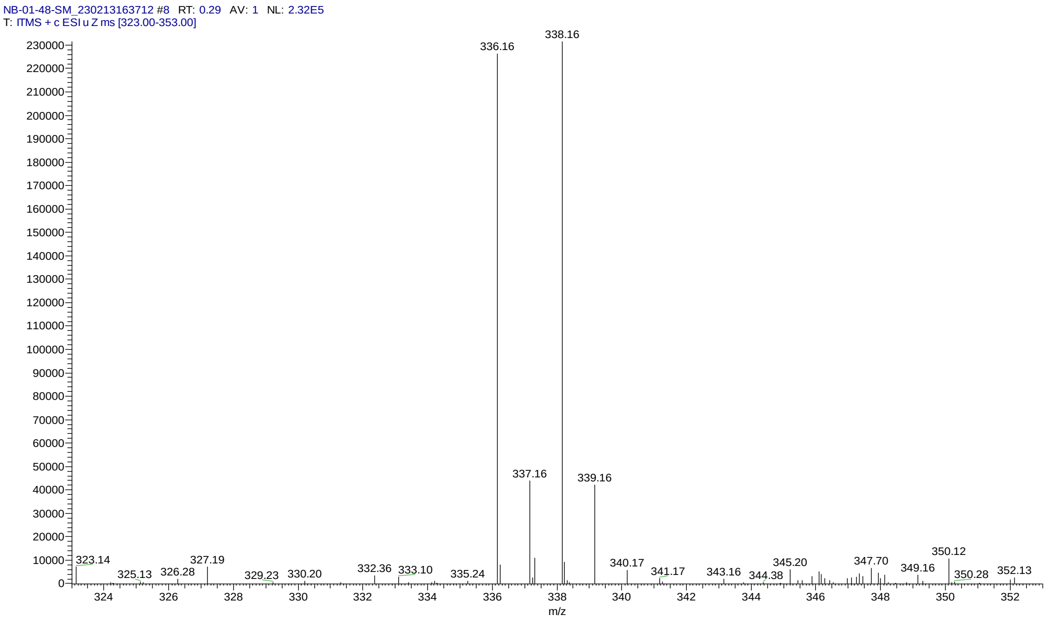
Expected derivatives: 14 | Labelled atoms: 13 | Atom%: 13.8 | Calculate

Unlabeled compound	Abundance	Analyte Abundance
M+1 462	274364.5	43986.629
M+2	40318.289	2040.0308
M+3	0	320468.13
M+4	0	31091.822
M+5	0	12724.425
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

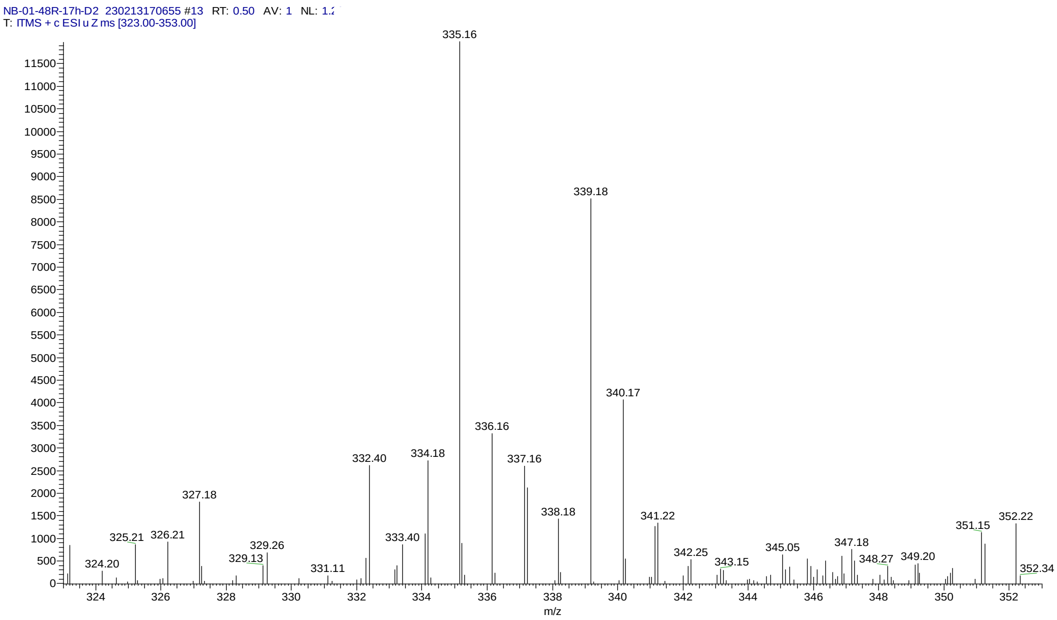


Results Relative amounts [%]			
unlabeled	12.3		
1-label	-1.2	1	-1.2
2-label	89.8	2	180
3-label	-4.5	3	-13
4-label	4.2	4	16.9
5-label	-0.6	5	-3.1
6-label	0.1	6	0.55
7-label	0.0	7	-0.1
8-label	0.0	8	0.02
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	1.79

Mass spectrum and isopat analysis of **9a**.



Mass spectrum of **10**.



Mass spectrum of **10a**.

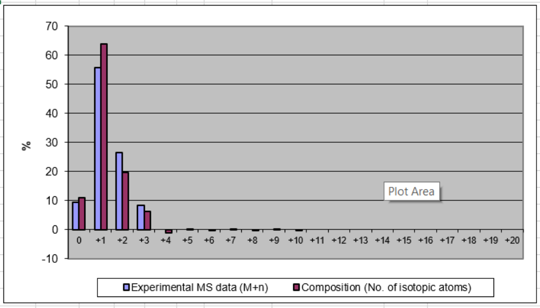
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	231578.44	1429.4752
M+2	42189.203	8518.4746
M+3	0	4062.752
M+4	0	1260.8884
M+5	0	0.00E+00
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14

Calculate

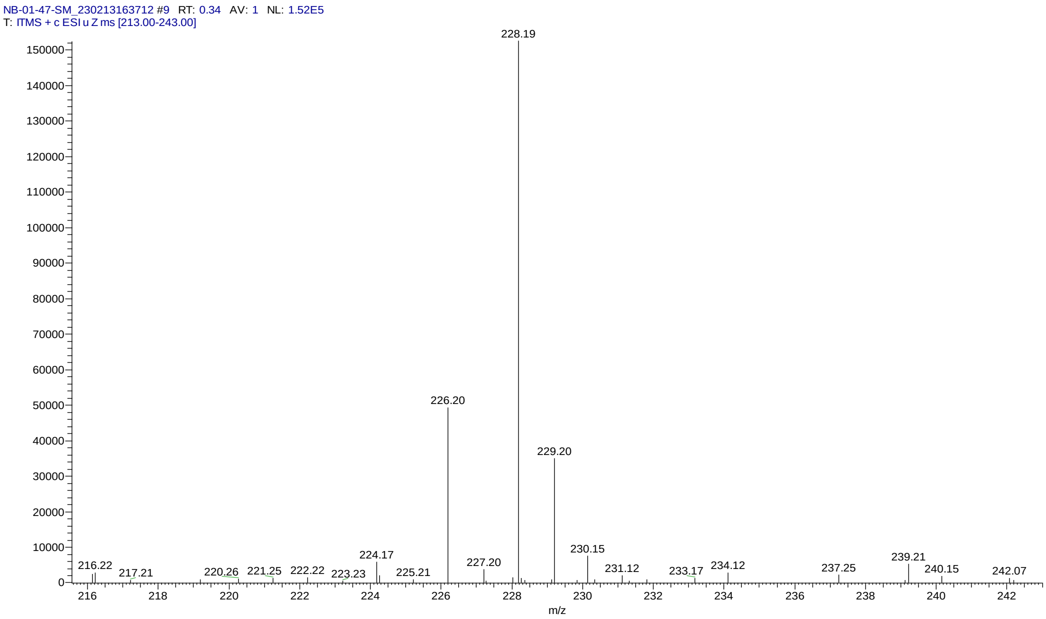
Labelled atoms 13

Atom% 9.1

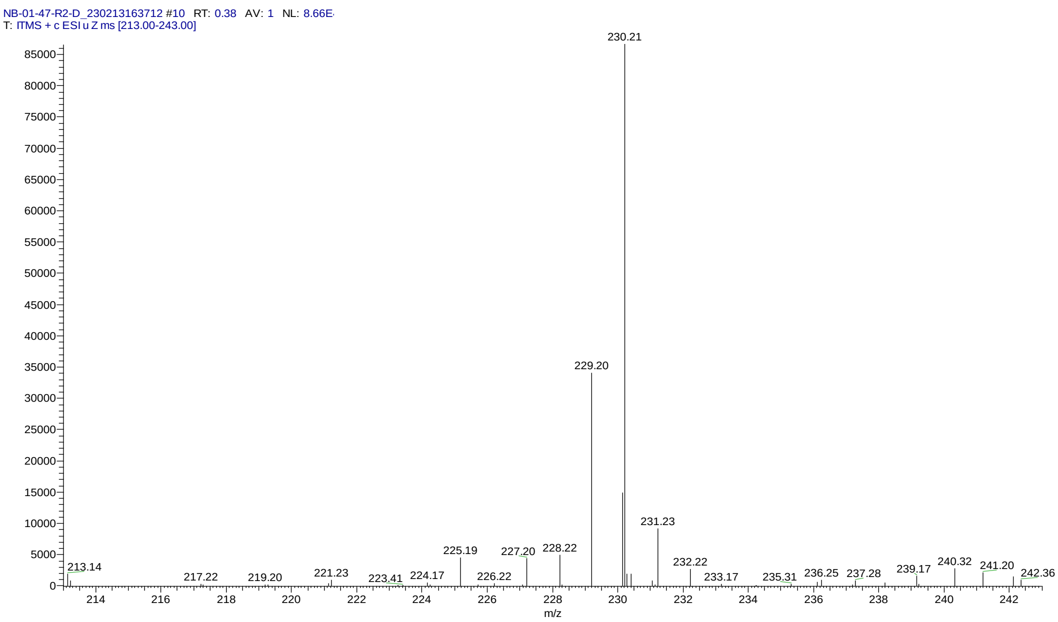


Results			
Relative amounts [%]			
unlabeled	11.1		
1-label	63.9	1	63.9
2-label	19.8	2	39.6
3-label	6.2	3	18.5
4-label	-1.1	4	-4.5
5-label	0.2	5	1.02
6-label	0.0	6	-0.2
7-label	0.0	7	0.05
8-label	0.0	8	-0
9-label	0.0	9	0
10-label	0.0	10	-0
11-label	0.0	11	0
12-label	0.0	12	-0
13-label	0.0	13	0
		Total:	1.18

Mass spectrum and isopat analysis of **10a**.



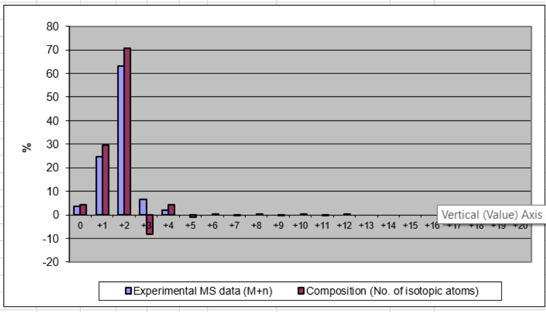
Mass spectrum of **11**.



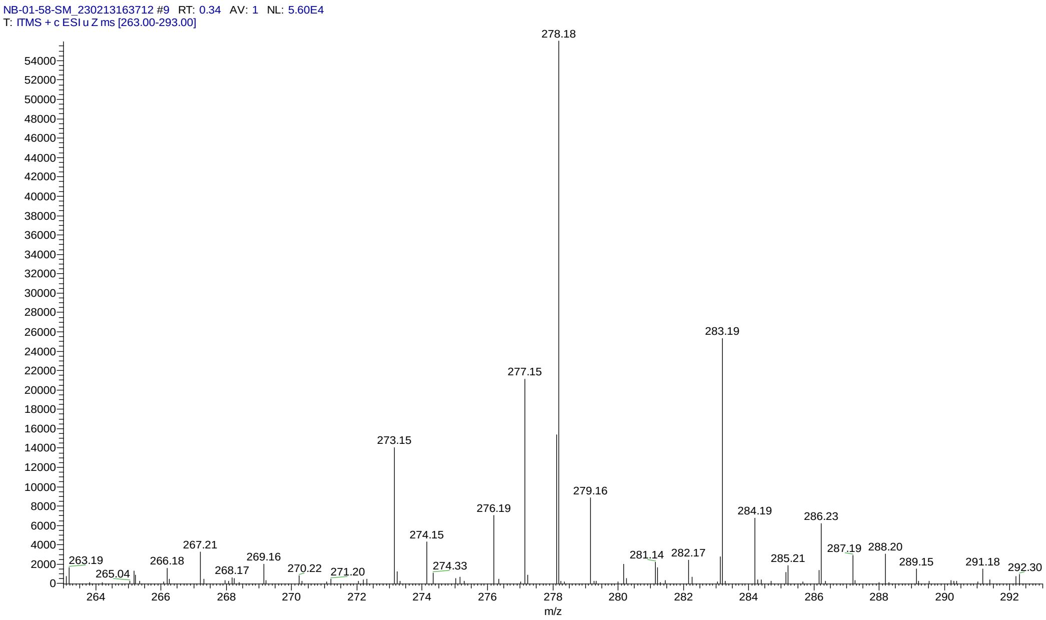
Mass spectrum of **11a**.

Expected derivatives: 14 | Labelled atoms 13 | Atom% 12.3 | Calculate

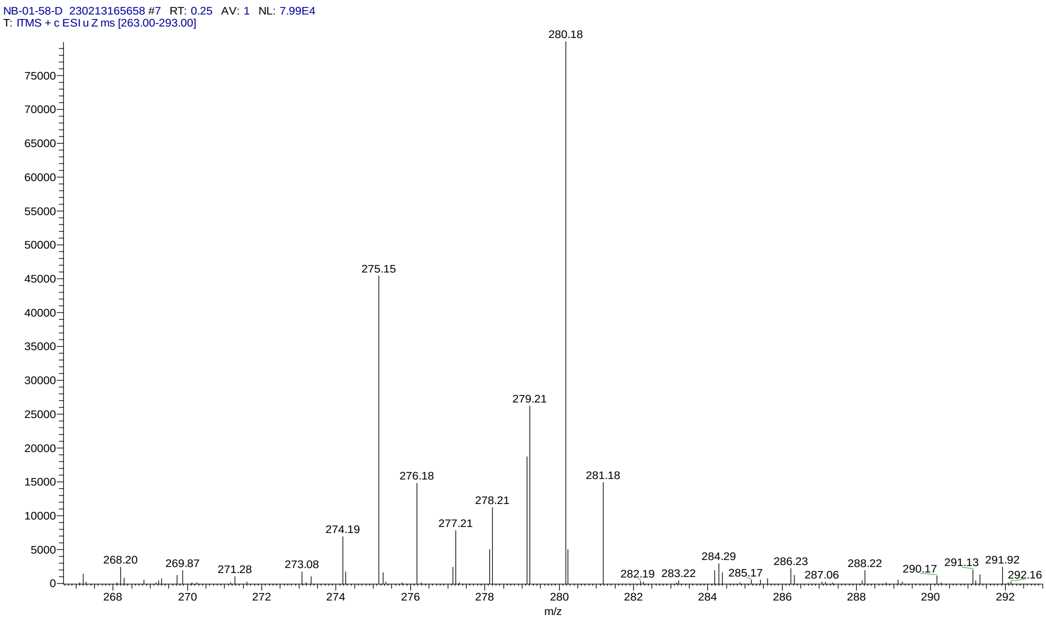
Unlabeled compound		Analyte	Results			
	Abundance	Abundance	Relative amounts [%]			
M+1 462	152421.47	4927.2358	unlabeled	4.4		
M+2	35007.617	33983.063	1-label	29.4	1	29.4
M+3	0	86580.016	2-label	70.8	2	142
M+4	0	9143.5811	3-label	-8.1	3	-24
M+5	0	2631.3521	4-label	4.2	4	16.8
M+6	0	0.00E+00	5-label	-1.0	5	-4.8
M+7	0	0	6-label	0.2	6	1.33
M+8	0	0	7-label	-0.1	7	-0.4
M+9	0	0	8-label	0.0	8	0.09
M+10	0	0	9-label	0.0	9	-0
M+11	0	0	10-label	0.0	10	0.01
M+12	0	0	11-label	0.0	11	-0
M+13	0	0	12-label	0.0	12	0
M+14	0	0	13-label	0.0	13	-0
	0	0			Total:	1.6
	0	0				
	0	0				
	0	0				
	0	0				
	0	0				



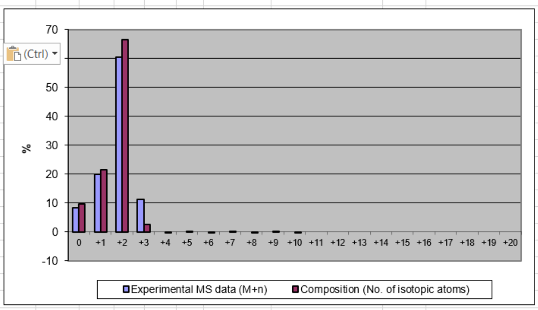
Mass spectrum and isopat analysis of **11a**.



Mass spectrum of **12**.



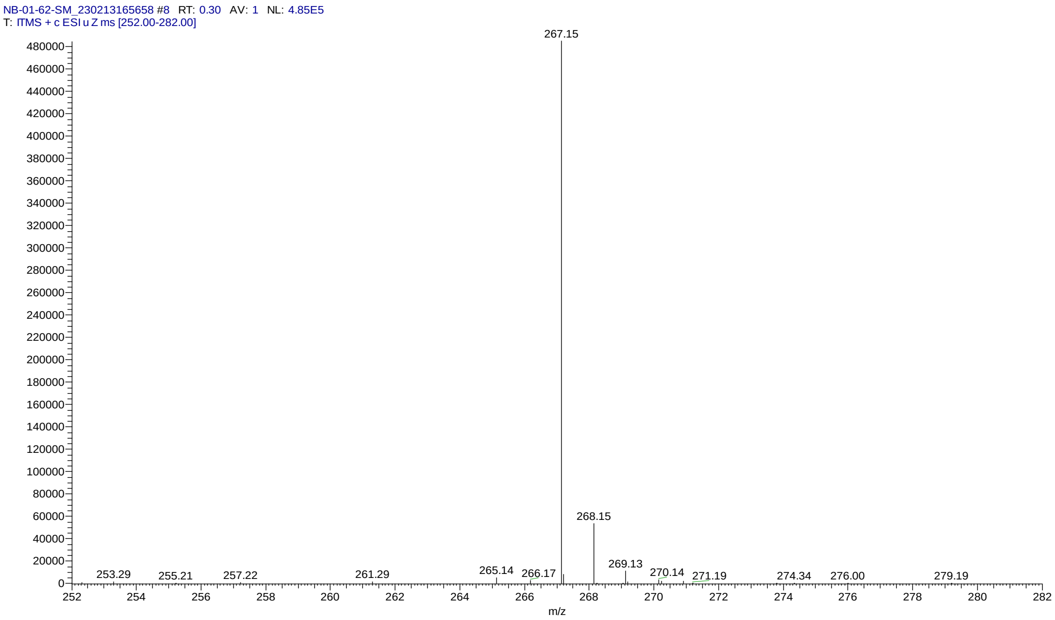
Mass spectrum of **12a**.



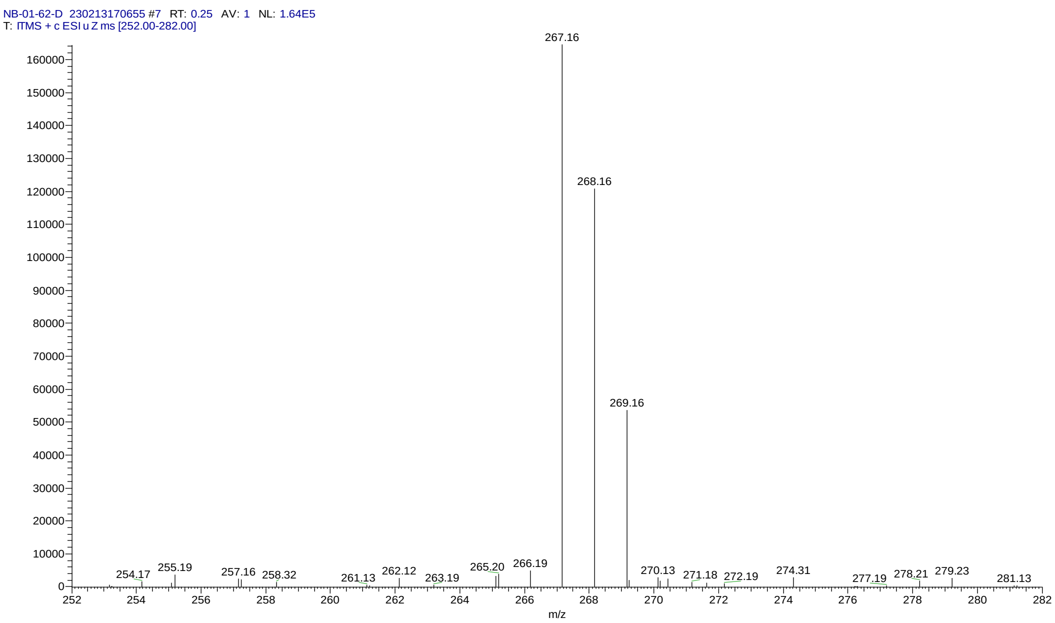
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	55985.695	11193.984
M+2	8880.4971	26215.146
M+3	0	79940.25
M+4	0	14934.639
M+5	0	0
M+6	0	0
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Results: Relative amounts [%]			
unlabeled	9.8		
1-label	21.4	1	21.4
2-label	66.6	2	133
3-label	2.5	3	7.54
4-label	-0.4	4	-1.6
5-label	0.1	5	0.32
6-label	0.0	6	-0.1
7-label	0.0	7	0.01
8-label	0.0	8	-0
9-label	0.0	9	0
10-label	0.0	10	-0
11-label	0.0	11	0
12-label	0.0	12	-0
13-label	0.0	13	0
		Total:	1.61

Mass spectrum and isopat analysis of **12a**.



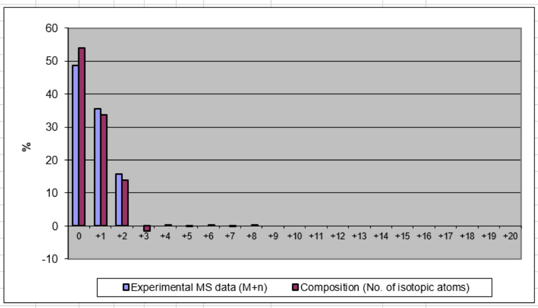
Mass spectrum of **13**.



Mass spectrum of **13a**.

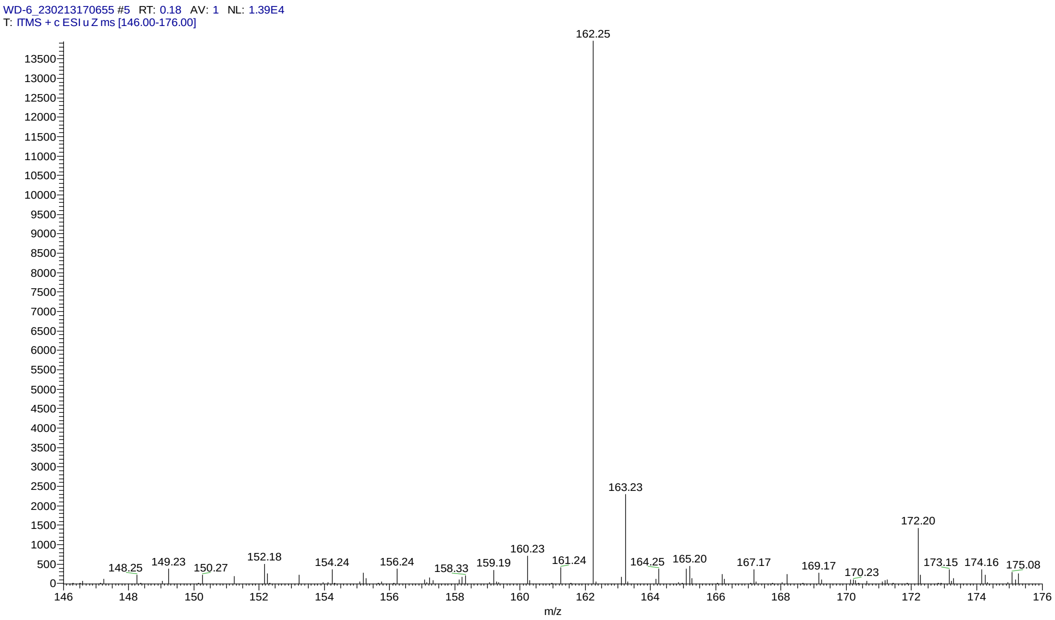
Unlabeled compound		Analyte
	Abundance	Abundance
M+1 462	484699.25	164385.8
M+2	53449.992	120665.85
M+3	0	53607.43
M+4	0	0.00E+00
M+5	0	0.00E+00
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives:	14	Labelled atoms	13
	Calculate	Atom%	4.4

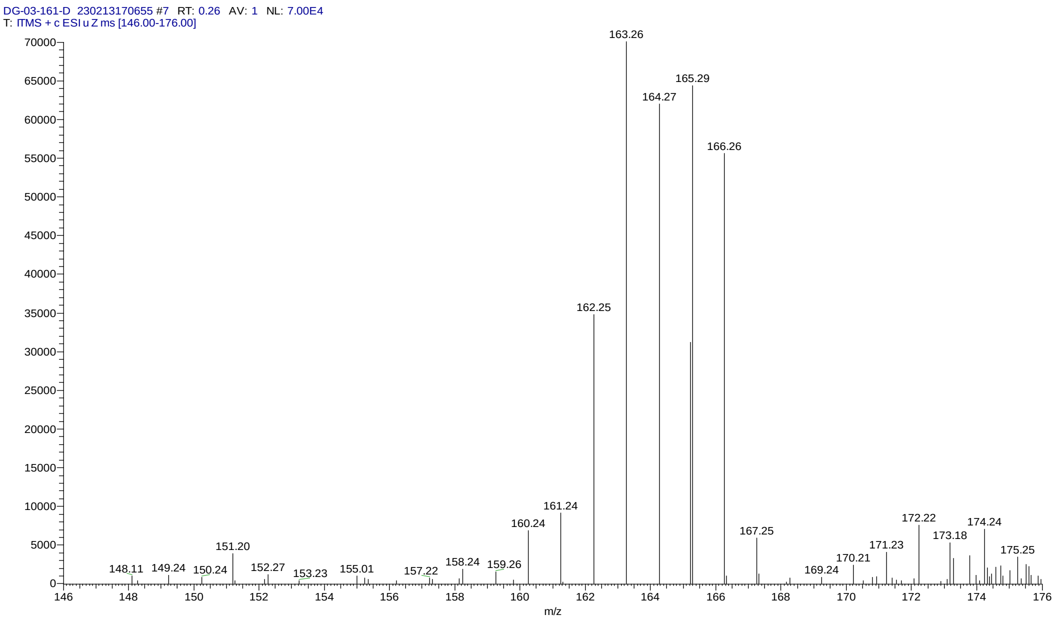


Results			
Relative amounts [%]			
unlabeled	53.9		
1-label	33.6	1	33.6
2-label	13.9	2	27.7
3-label	-1.5	3	-4.6
4-label	0.2	4	0.67
5-label	0.0	5	-0.1
6-label	0.0	6	0.01
7-label	0.0	7	-0
8-label	0.0	8	0
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	0.57

Mass spectrum and isopat analysis of **13a**.



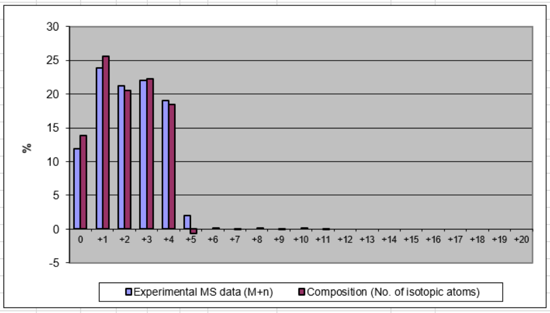
Mass spectrum of **14**.



Mass spectrum of **14a**.

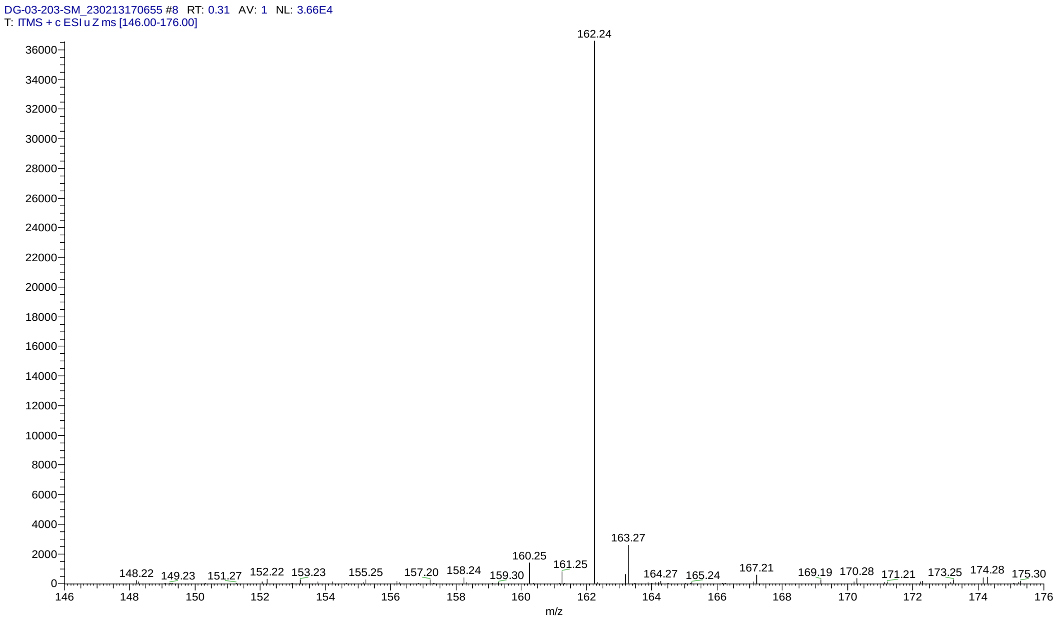
Expected derivatives: 14 | Labelled atoms: 13 | Atom%: 15.7 | Calculate

Unlabeled compound	Abundance	Analyte Abundance
M+1 462	13949.02	34751.531
M+2	2291.2432	70002.656
M+3	0	62034.336
M+4	0	64345.891
M+5	0	55608.789
M+6	0	5914.9595
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

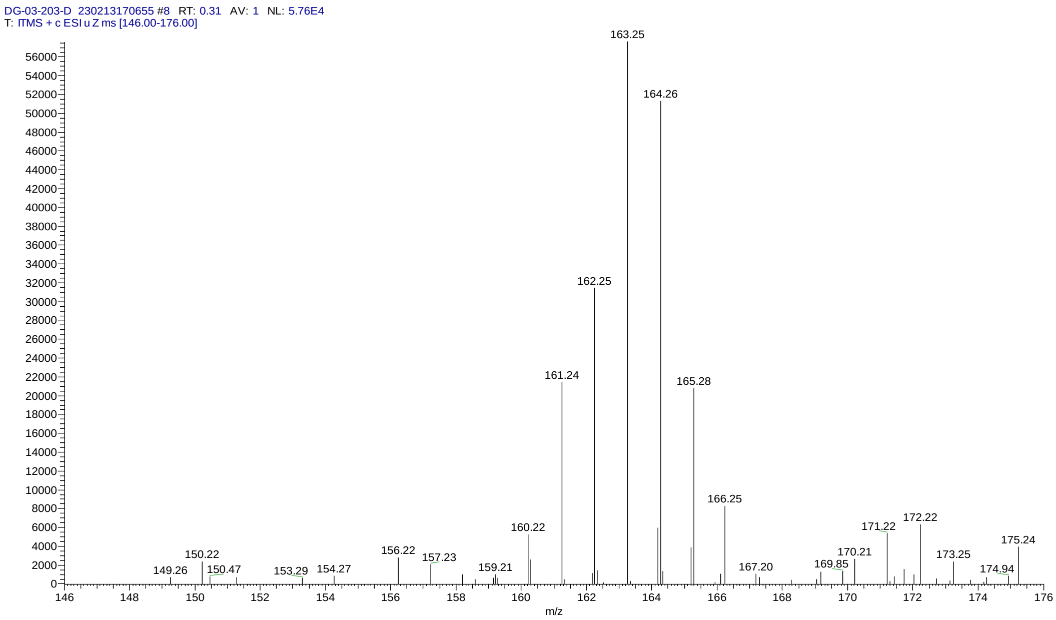


Results Relative amounts [%]			
unlabeled	13.8		
1-label	25.6	1	25.6
2-label	20.5	2	41
3-label	22.2	3	66.7
4-label	18.5	4	73.9
5-label	-0.7	5	-3.4
6-label	0.1	6	0.67
7-label	0.0	7	-0.1
8-label	0.0	8	0.02
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	2.04

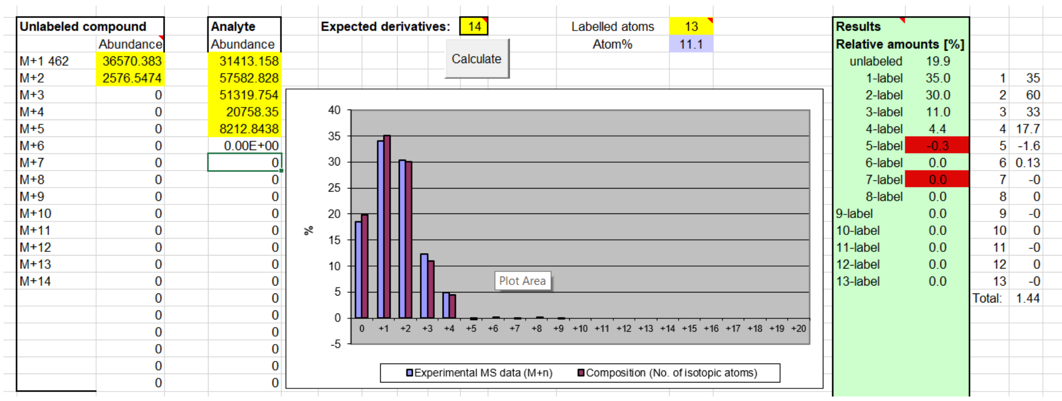
Mass spectrum and isopat analysis of **14a**.



Mass spectrum of **15**.



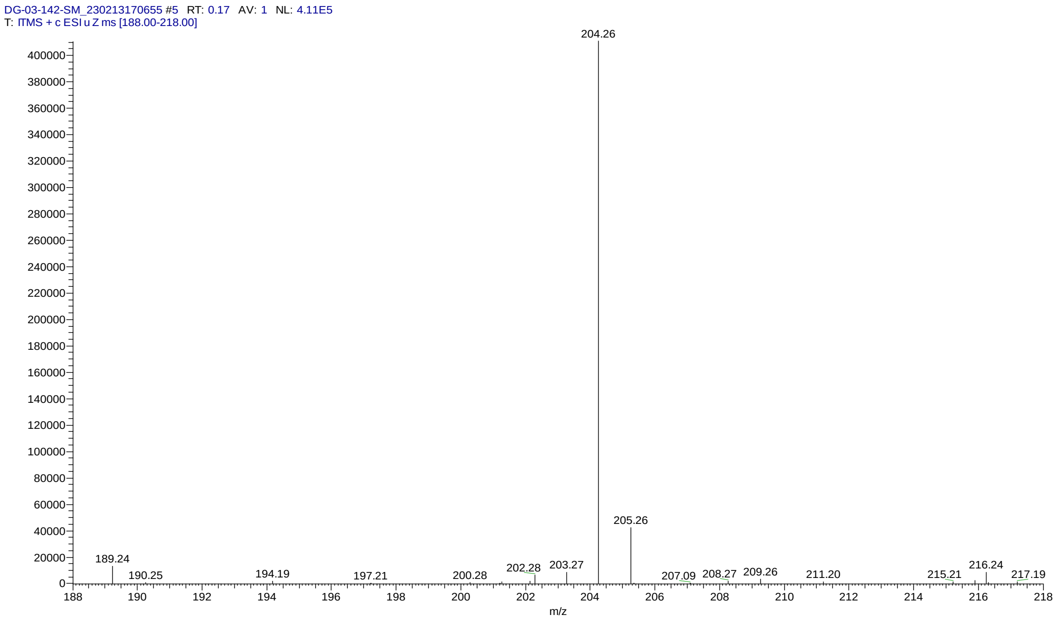
Mass spectrum of **15a**.



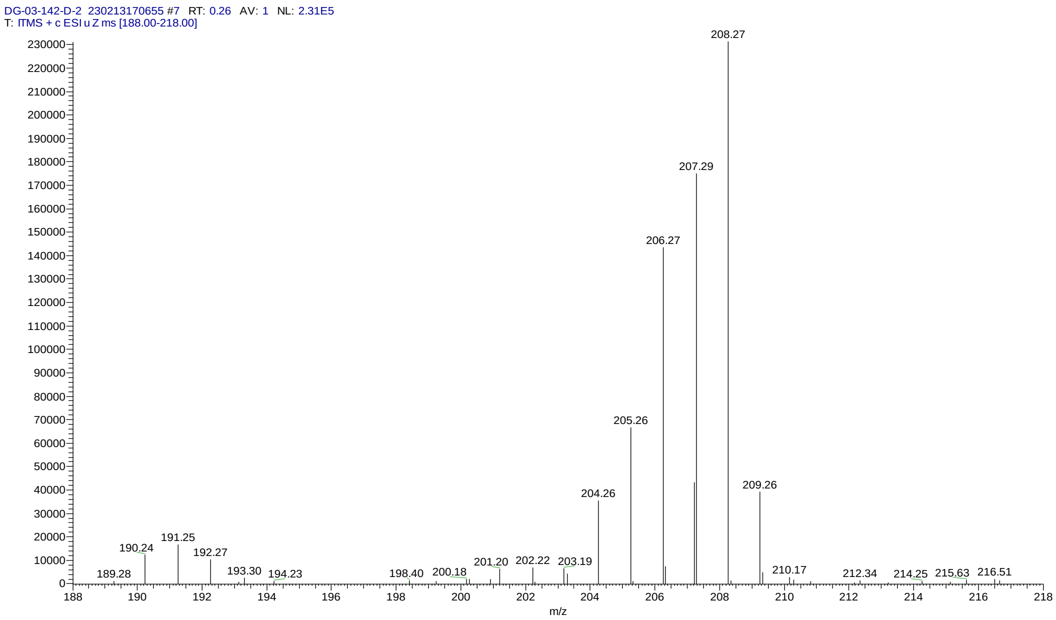
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	36570.383	31413.158
M+2	2576.5474	57582.828
M+3	0	51319.754
M+4	0	20758.35
M+5	0	8212.8438
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Results Relative amounts [%]			
unlabeled	19.9		
1-label	35.0	1	35
2-label	30.0	2	60
3-label	11.0	3	33
4-label	4.4	4	17.7
5-label	-0.3	5	-1.6
6-label	0.0	6	0.13
7-label	0.0	7	-0
8-label	0.0	8	0
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	1.44

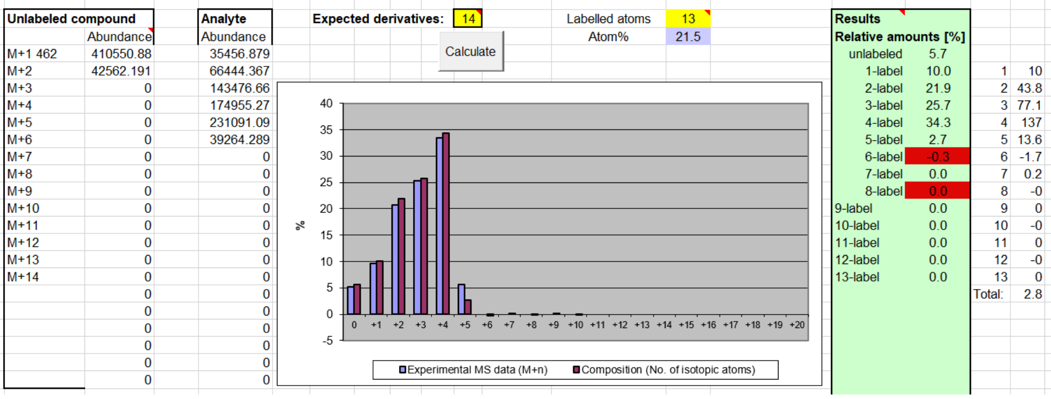
Mass spectrum and isopat analysis of **15a**.



Mass spectrum of **16**.



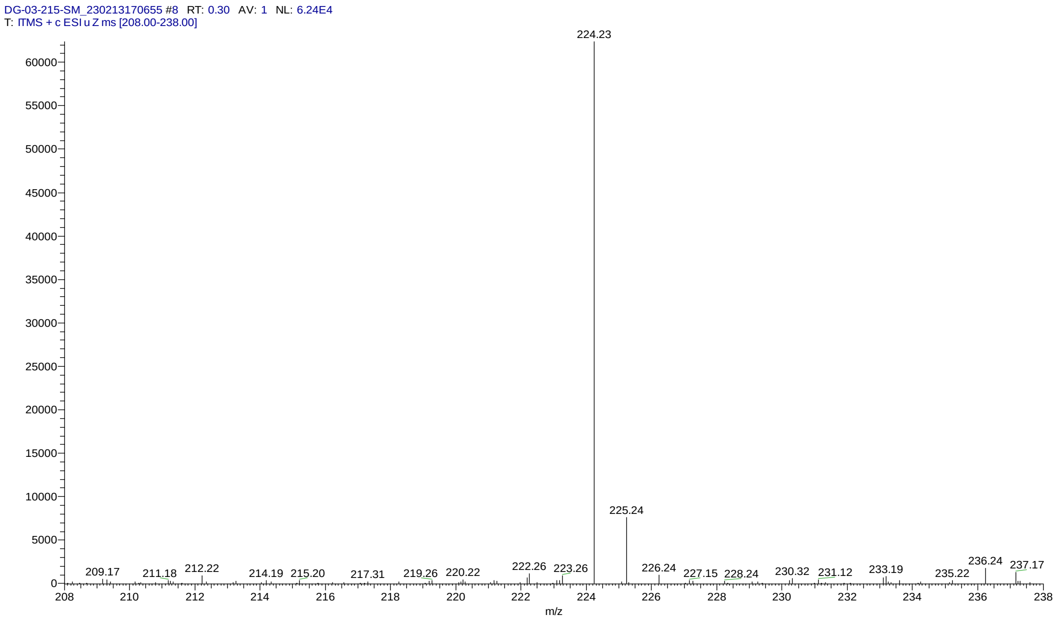
Mass spectrum of **16a**.



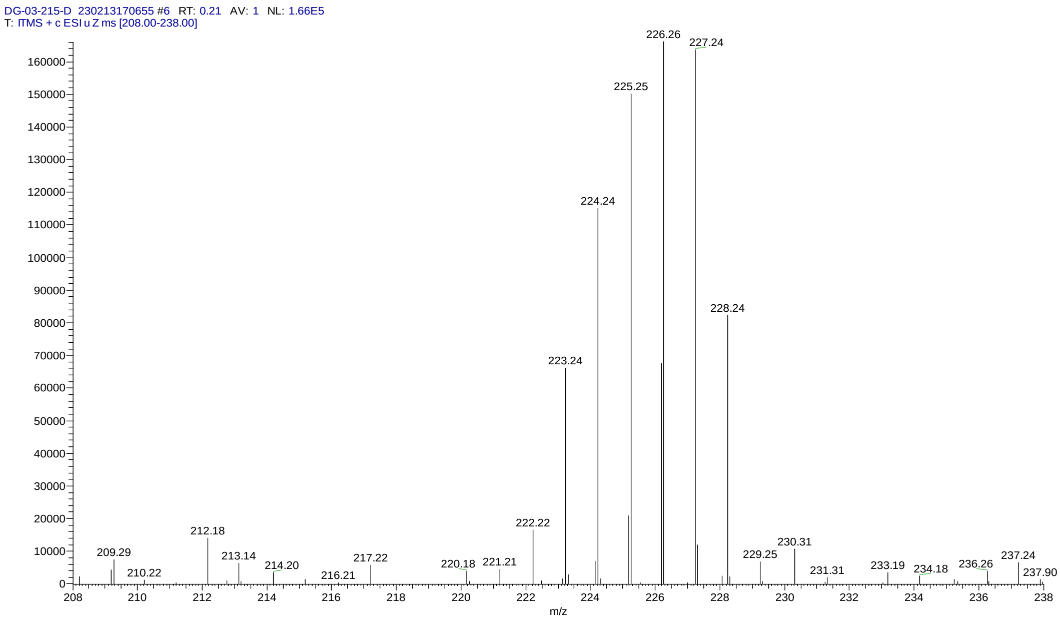
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	410550.88	35456.879
M+2	42562.191	66444.367
M+3	0	143476.66
M+4	0	174955.27
M+5	0	231091.09
M+6	0	39264.289
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Results – Relative amounts [%]			
unlabeled	5.7		
1-label	10.0	1	10
2-label	21.9	2	43.8
3-label	25.7	3	77.1
4-label	34.3	4	137
5-label	2.7	5	13.6
6-label	-0.3	6	-1.7
7-label	0.0	7	0.2
8-label	0.0	8	-0
9-label	0.0	9	0
10-label	0.0	10	-0
11-label	0.0	11	0
12-label	0.0	12	-0
13-label	0.0	13	0
		Total:	2.8

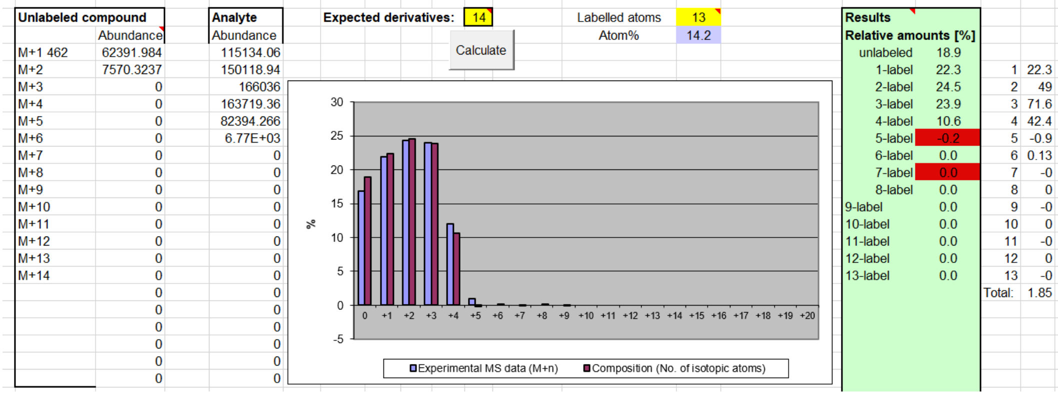
Mass spectrum and isopat analysis of **16a**.



Mass spectrum of **17**.



Mass spectrum of **17a**.

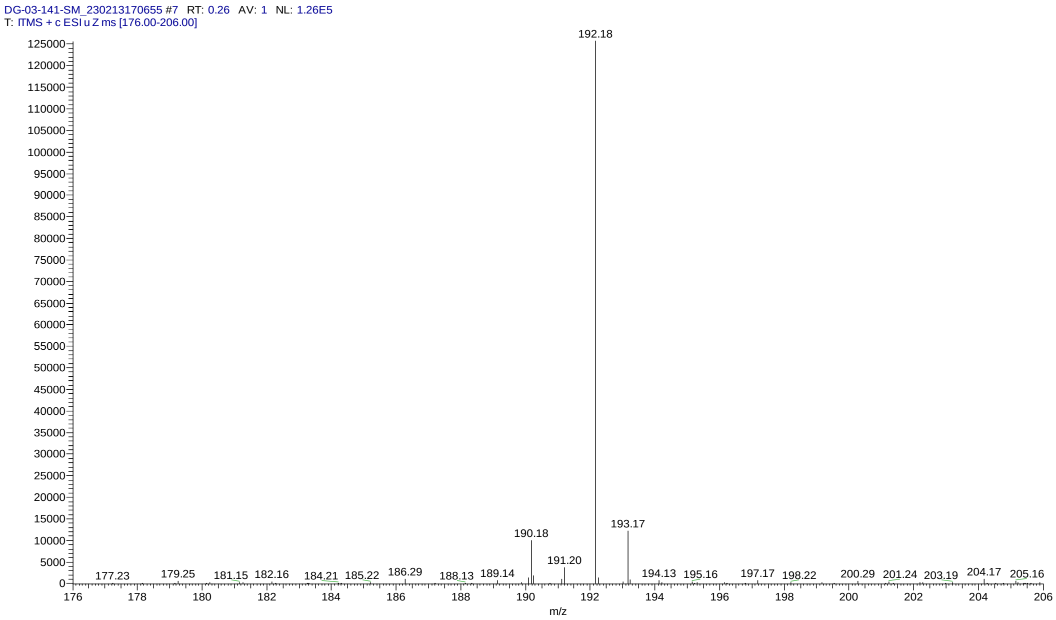


Unlabeled compound		Analyte
	Abundance	Abundance
M+1 462	62391.984	115134.06
M+2	7570.3237	150118.94
M+3	0	166036
M+4	0	163719.36
M+5	0	82394.266
M+6	0	6.77E+03
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

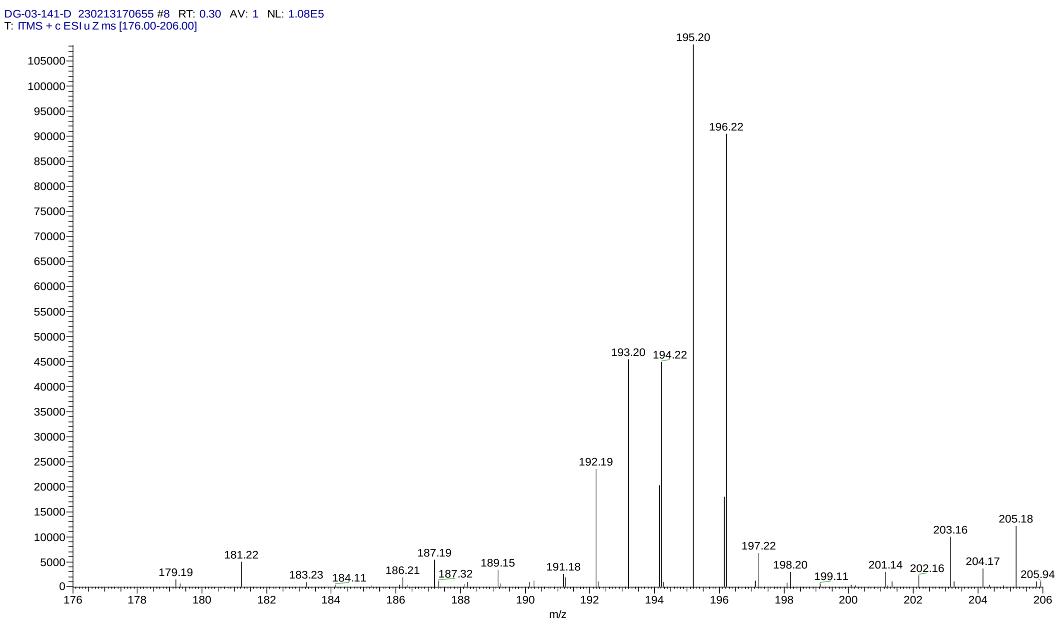
Expected derivatives: 14 | Calculate | Labelled atoms: 13 | Atom%: 14.2

Results			
Relative amounts [%]			
unlabeled	18.9		
1-label	22.3	1	22.3
2-label	24.5	2	49
3-label	23.9	3	71.6
4-label	10.6	4	42.4
5-label	-0.2	5	-0.9
6-label	0.0	6	0.13
7-label	0.0	7	-0
8-label	0.0	8	0
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	1.85

Mass spectrum and isopat analysis of **17a**.



Mass spectrum of **18**.

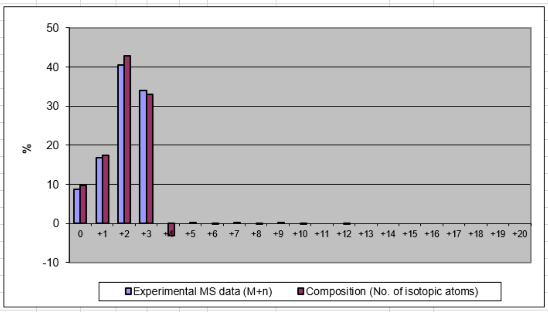


Mass spectrum of **18a**.

Unlabeled compound		Analyte
	Abundance	Abundance
M+1 462	125621.66	23493.336
M+2	12214.594	44802.992
M+3	0	108223.39
M+4	0	90501.375
M+5	0	0
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

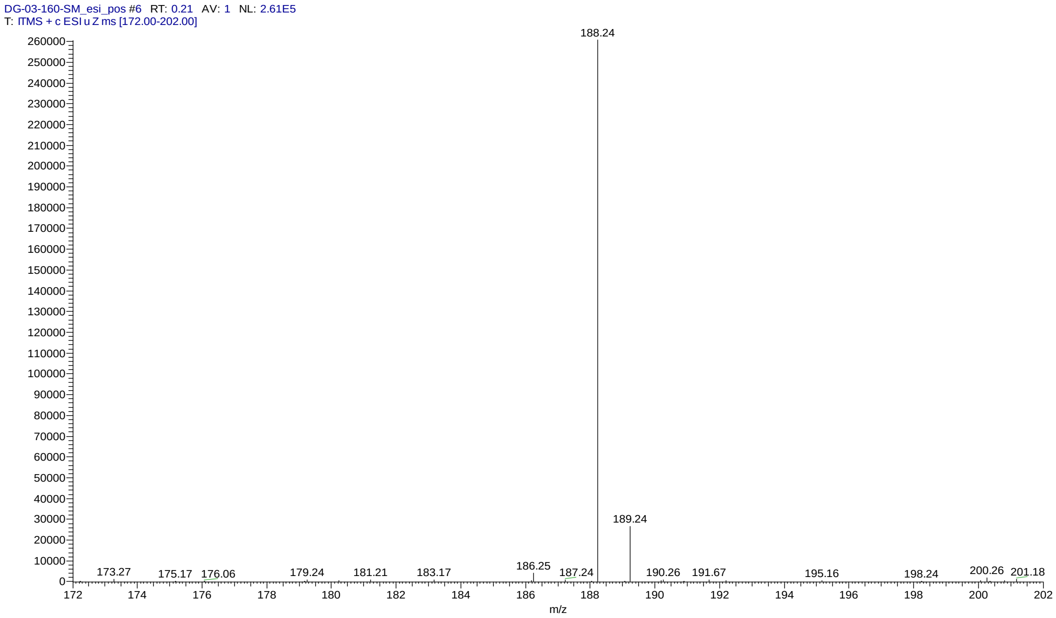
Expected derivatives: 14 | Labelled atoms 13 | Atom% 14.7

Calculate

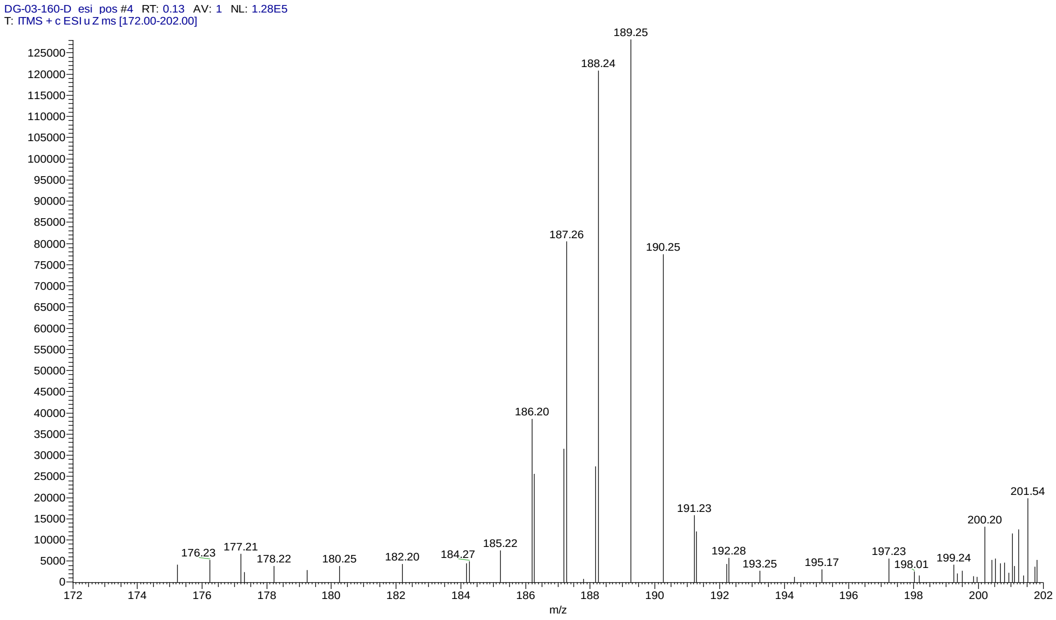


Results			
Relative amounts [%]			
unlabeled	9.7		
1-label	17.5	1	17.5
2-label	42.8	2	85.5
3-label	33.0	3	99.1
4-label	-3.2	4	-13
5-label	0.3	5	1.56
6-label	0.0	6	-0.2
7-label	0.0	7	0.02
8-label	0.0	8	-0
9-label	0.0	9	0
10-label	0.0	10	-0
11-label	0.0	11	0
12-label	0.0	12	-0
13-label	0.0	13	0
		Total:	1.91

Mass spectrum and isopat analysis of **18a**.



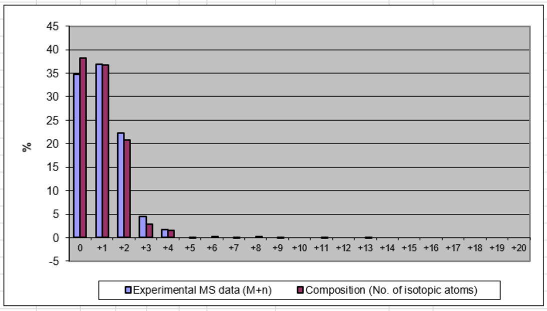
Mass spectrum of **19**.



Mass spectrum of **19a**.

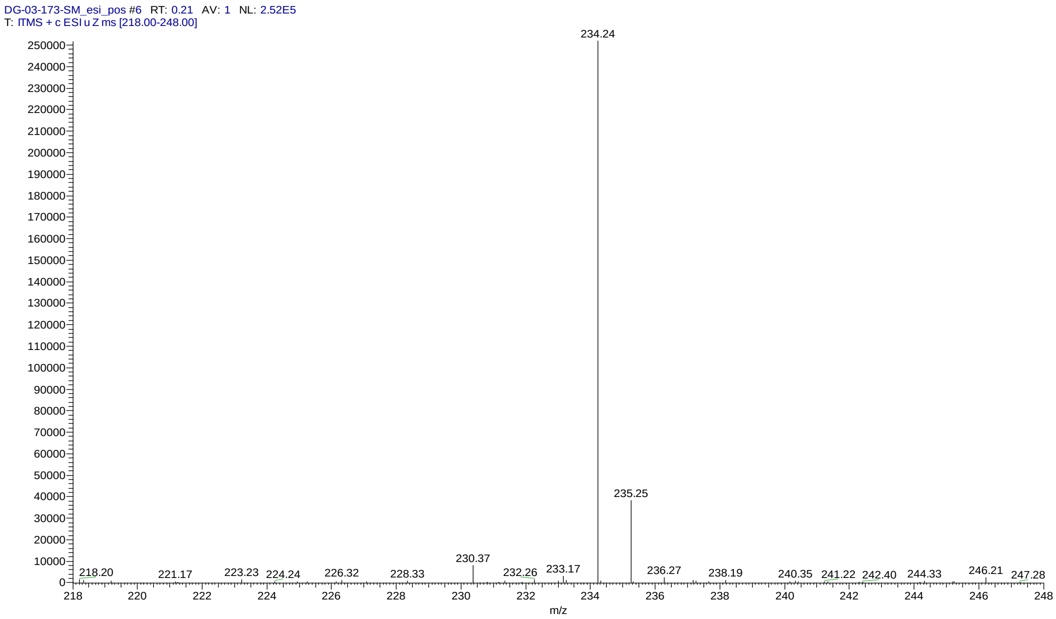
Unlabeled compound		Analyte
	Abundance	Abundance
M+1 462	260517.25	120746.55
M+2	26521.164	128020.61
M+3	0	77422.859
M+4	0	15831.836
M+5	0	5716.6333
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives:	14	Labelled atoms	13
Calculate		Atom%	7.1

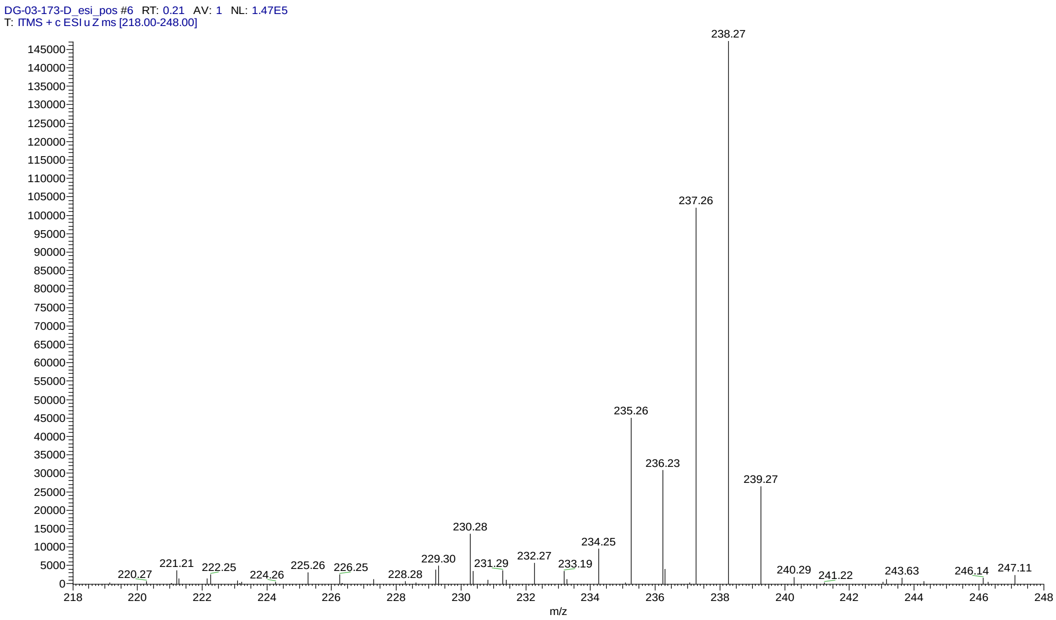


Results			
Relative amounts [%]			
unlabeled	38.3		
1-label	36.7	1	36.7
2-label	20.8	2	41.6
3-label	2.9	3	8.7
4-label	1.5	4	6.06
5-label	-0.2	5	-0.8
6-label	0.0	6	0.09
7-label	0.0	7	-0
8-label	0.0	8	0
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	0.92

Mass spectrum and isopat analysis of **19a**.



Mass spectrum of **20**.



Mass spectrum of **20a**.

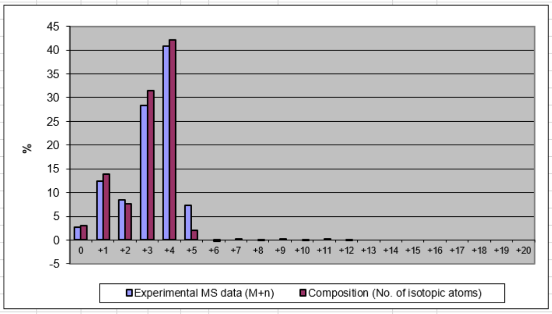
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	251756.58	9454.9395
M+2	38385.742	44864.328
M+3	0	30741.02
M+4	0	102021.31
M+5	0	147072.5
M+6	0	26341.629
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14

Calculate

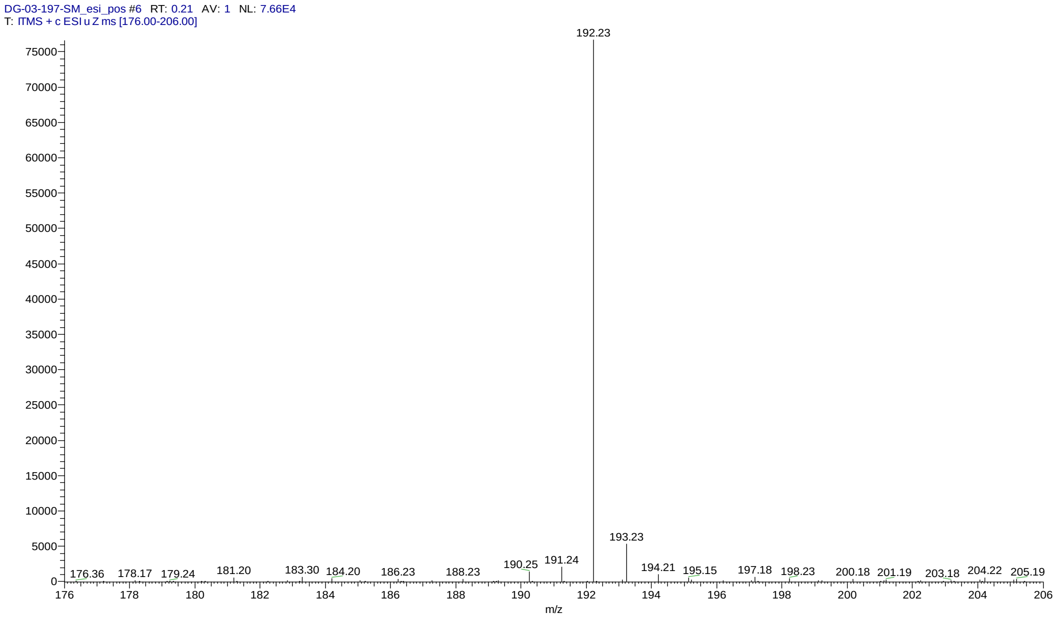
Labelled atoms 13

Atom% 23.1

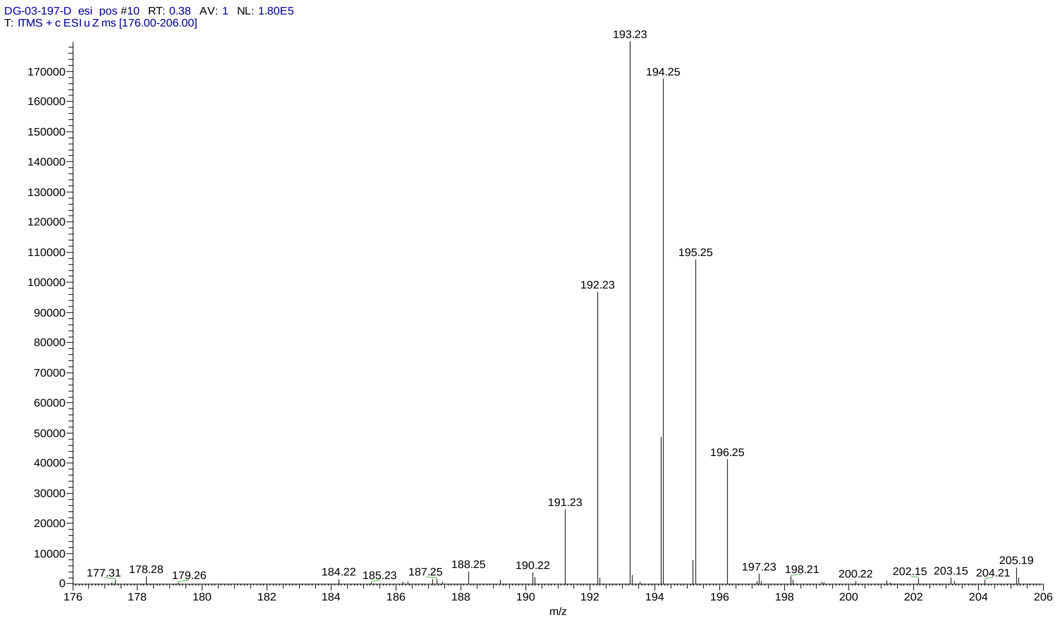


Results Relative amounts [%]			
unlabeled	3.0		
1-label	13.9	1	13.9
2-label	7.7	2	15.4
3-label	31.4	3	94.3
4-label	42.2	4	169
5-label	2.0	5	9.92
6-label	-0.3	6	-1.8
7-label	0.0	7	0.32
8-label	0.0	8	-0.1
9-label	0.0	9	0.01
10-label	0.0	10	-0
11-label	0.0	11	0
12-label	0.0	12	-0
13-label	0.0	13	0
		Total:	3.01

Mass spectrum and isopat analysis of **20a**.



Mass spectrum of **21**.



Mass spectrum of **21a**.

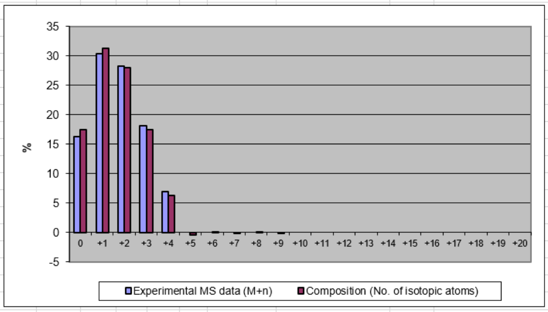
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	76626.391	96743.797
M+2	5291.2456	179735.23
M+3	0	167413.8
M+4	0	107449.11
M+5	0	41232.953
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14

Labelled atoms: 13

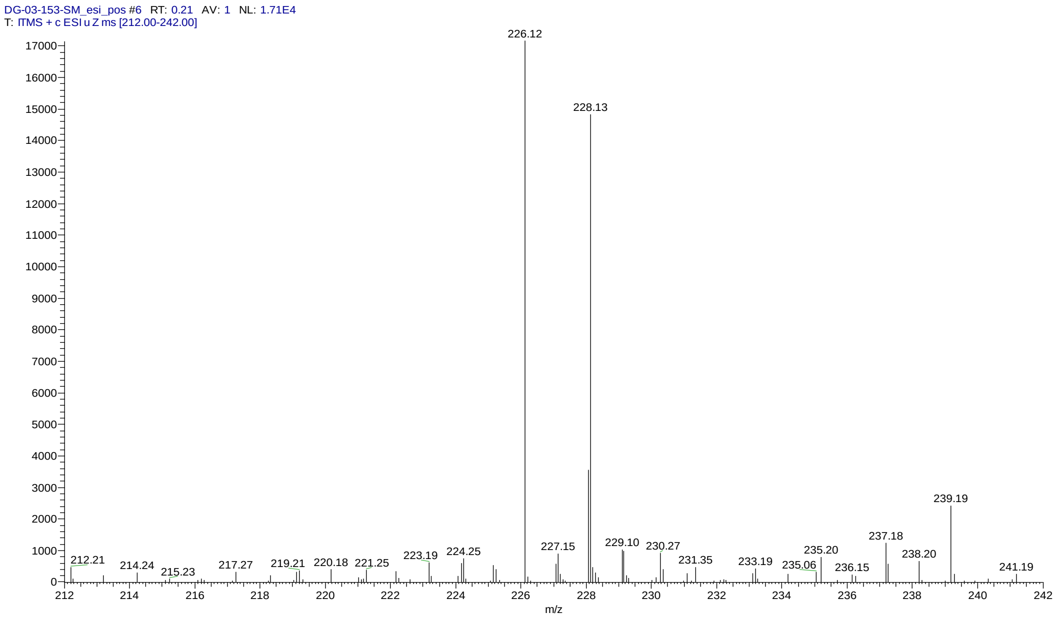
Atom%: 12.5

Calculate

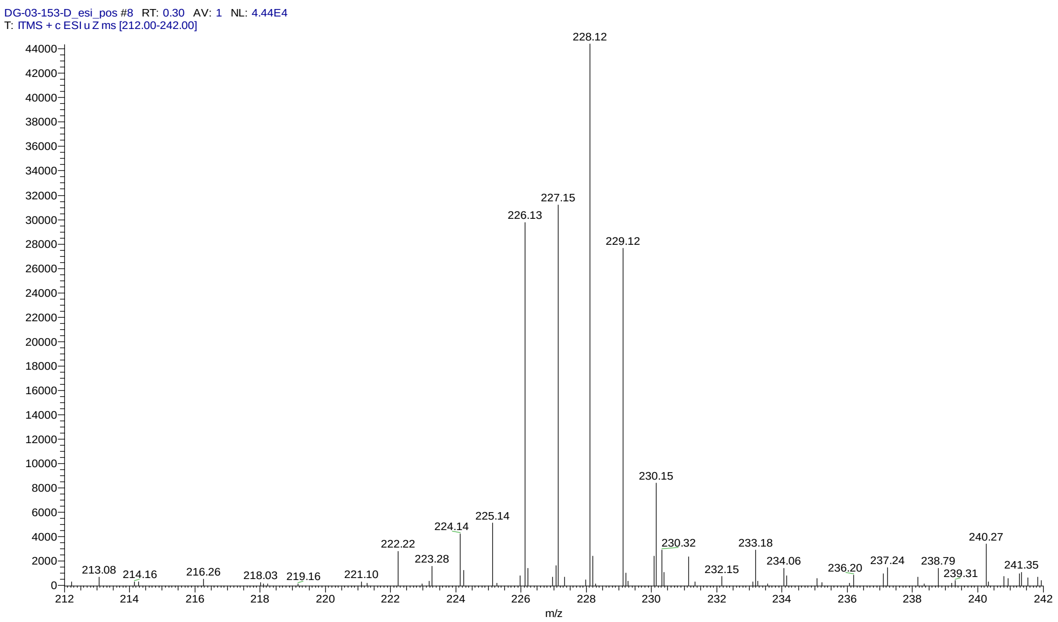


Results: Relative amounts [%]			
unlabeled	17.5		
1-label	31.2	1	31.2
2-label	28.0	2	56.1
3-label	17.4	3	52.3
4-label	6.2	4	24.9
5-label	-0.4	5	-2.2
6-label	0.0	6	0.18
7-label	0.0	7	-0
8-label	0.0	8	0
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	1.63

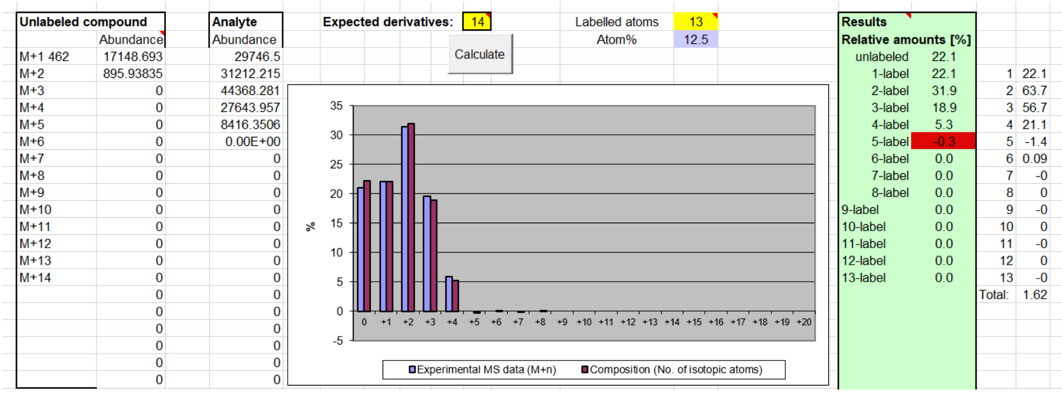
Mass spectrum and isopat analysis of **21a**.



Mass spectrum of **22**.

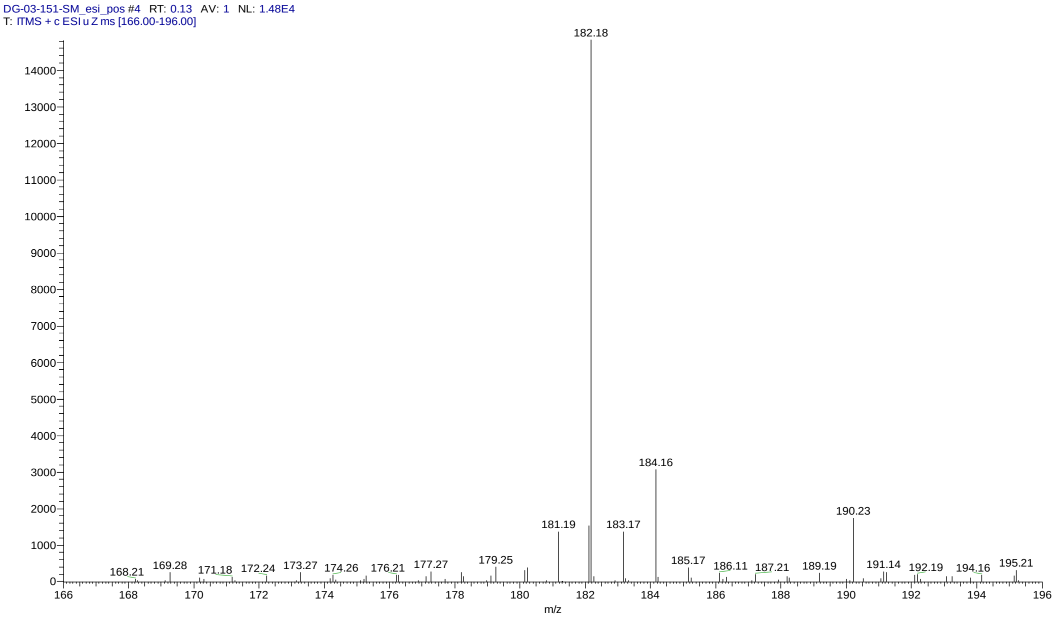


Mass spectrum of **22a**.

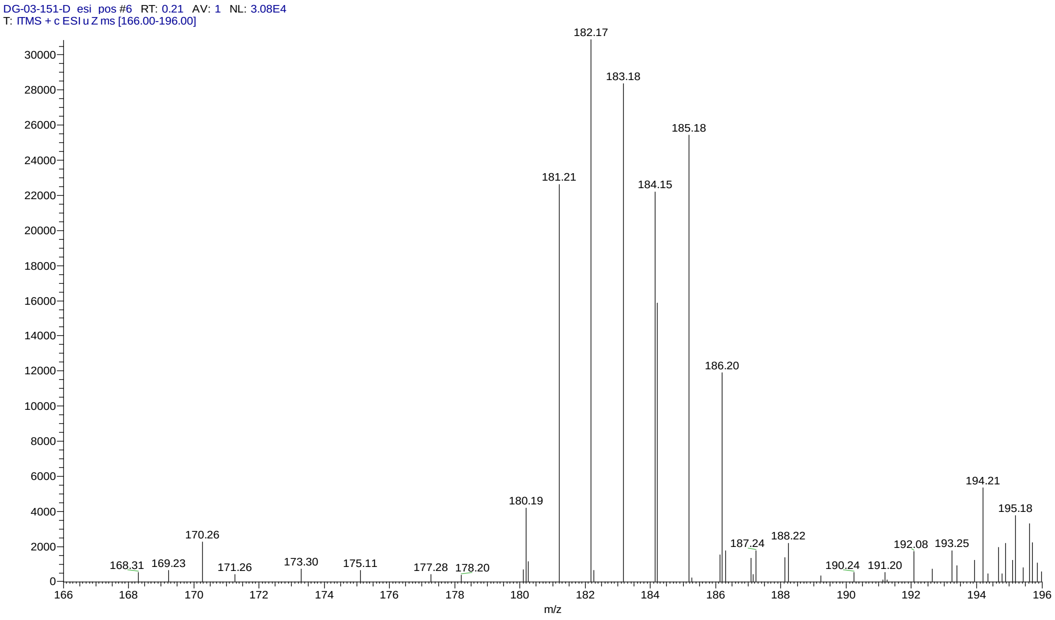


Unlabeled compound	Abundance	Analyte Abundance	Results Relative amounts [%]			
M+1 462	17148.693	29746.5	unlabeled	22.1		
M+2	895.93835	31212.215	1-label	22.1	1	22.1
M+3	0	44368.281	2-label	31.9	2	63.7
M+4	0	27643.957	3-label	18.9	3	56.7
M+5	0	8416.3506	4-label	5.3	4	21.1
M+6	0	0.00E+00	5-label	-0.3	5	-1.4
M+7	0	0	6-label	0.0	6	0.09
M+8	0	0	7-label	0.0	7	-0
M+9	0	0	8-label	0.0	8	0
M+10	0	0	9-label	0.0	9	-0
M+11	0	0	10-label	0.0	10	0
M+12	0	0	11-label	0.0	11	-0
M+13	0	0	12-label	0.0	12	0
M+14	0	0	13-label	0.0	13	-0
	0	0			Total:	1.62
	0	0				
	0	0				
	0	0				
	0	0				
	0	0				

Mass spectrum and isopat analysis of **22a**.



Mass spectrum of **23**.



Mass spectrum of **23a**.

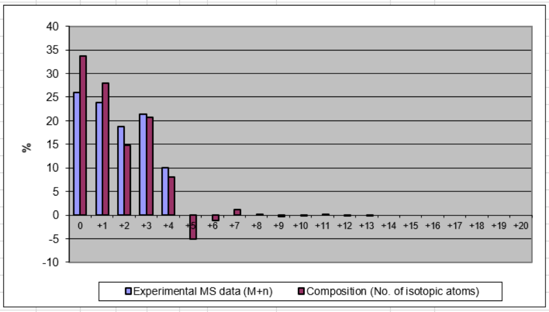
Unlabeled compound	Abundance	Analyte Abundance
M+1 462	14819.599	30848.029
M+2	1352.9835	28345.066
M+3	3071.1694	22183.363
M+4	0	25414.656
M+5	0	11907.202
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14

Calculate

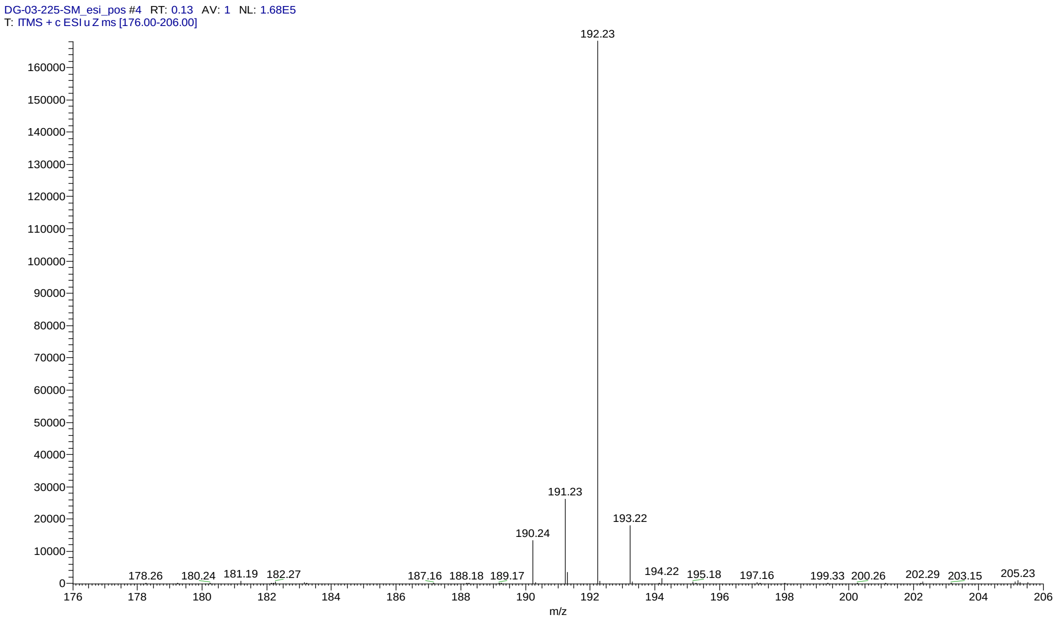
Labelled atoms 13

Atom% 9.7

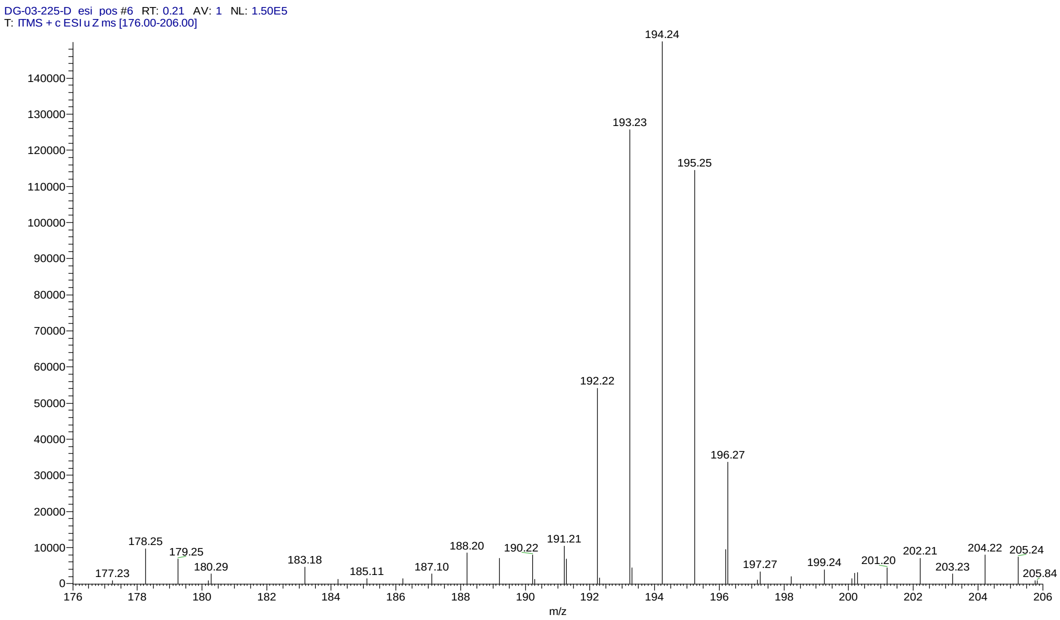


Results			
Relative amounts [%]			
unlabeled	33.7		
1-label	27.9	1	27.9
2-label	14.7	2	29.5
3-label	20.7	3	62
4-label	8.1	4	32.4
5-label	-5.0	5	-25
6-label	-1.2	6	-7.3
7-label	1.2	7	8.06
8-label	0.1	8	1.18
9-label	-0.3	9	-2.3
10-label	0.0	10	-0.1
11-label	0.1	11	0.58
12-label	0.0	12	-0
13-label	0.0	13	-0.1
		Total:	1.27

Mass spectrum and isopat analysis of **23a**.



Mass spectrum of **24**.

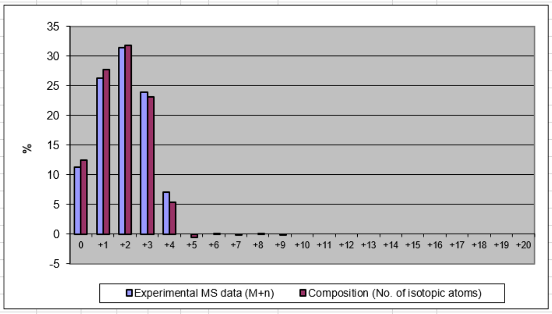


Mass spectrum of **24a**.

Unlabeled compound	Abundance	Analyte Abundance
M+1 462	168123.13	54072.672
M+2	17985.35	125664.73
M+3	0	149972.06
M+4	0	114535.47
M+5	0	33634.445
M+6	0	0.00E+00
M+7	0	0
M+8	0	0
M+9	0	0
M+10	0	0
M+11	0	0
M+12	0	0
M+13	0	0
M+14	0	0
	0	0
	0	0
	0	0
	0	0
	0	0
	0	0

Expected derivatives: 14 | Labelled atoms 13 | Atom% 13.8

Calculate



Results Relative amounts [%]			
unlabeled	12.5		
1-label	27.8	1	27.8
2-label	31.8	2	63.5
3-label	23.1	3	69.4
4-label	5.3	4	21.3
5-label	-0.6	5	-2.8
6-label	0.1	6	0.37
7-label	0.0	7	-0
8-label	0.0	8	0.01
9-label	0.0	9	-0
10-label	0.0	10	0
11-label	0.0	11	-0
12-label	0.0	12	0
13-label	0.0	13	-0
		Total:	1.79

Mass spectrum and isopat analysis of **24a**.