Diversity-Oriented Synthesis of Cyclophanes *via* Photo-Fries-type Rearrangement of *N*-Aryl Lactams.

Piotr Szcześniak* and Bartłomiej Furman*

Institute of Organic Chemistry, Polish Academy of Sciences

Kasprzaka 44/52, 01-224 Warsaw, Poland

Corresponding authors: pszczesniak@icho.edu.pl bfurman@icho.edu.pl

Table of Context:

1. General information:

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400, Varian VNMRS 500 and Varian VNMRS 600 spectrometers. ^{1}H NMR spectra were referenced to: chloroform-*d* (δ = 7.26 ppm), benzene d_6 (δ = 7.16 ppm), methanol-d_4 (δ = 3.31 ppm), DMSO-d_6 (δ = 2.50 ppm), ^{13}C NMR spectra were referenced to: chloroform-*d* (δ = 77.16 ppm), benzene-d_6 (δ = 128.06 ppm), methanol-d_4 (δ = 49.00 ppm), DMSO-d_6 (δ = 39.52 ppm). Chemical shifts (δ) were given in ppm and coupling constants (*J*) were given in Hertz (Hz). Multiplicity was indicated as follows: s (singlet), bs (brought singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet). Infrared spectra were recorded on a FT-IR Jasco 6200 and FT-IR Spectrum 2000 Perkin Elmer spectrophotometer. High-resolution mass spectra were recorded on ESI-TOF Mariner Spectrometer, SYNAPT G2-S HDMS or AMD 604 mass spectrometer. Thin layer chromatography was performed on Merck aluminium sheet Silica Gel 60 F254. Column chromatography was carried out using Merck silica gel (230-400 mesh).

2. Photochemical reaction in batch.

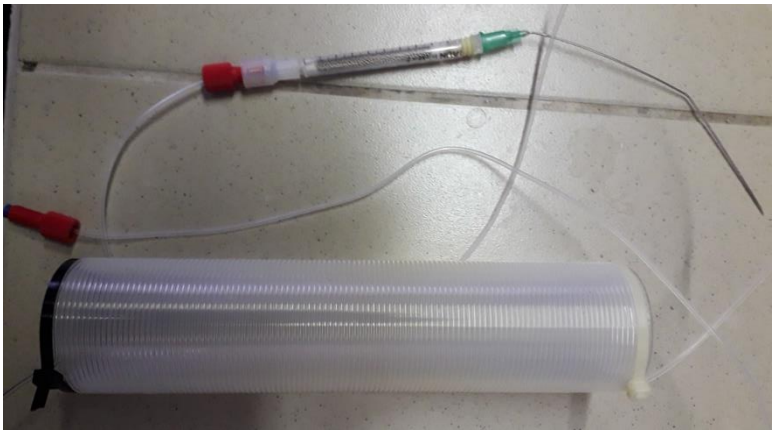
Photochemical reactions in bath were performed in Rayonet-type, self-made photoreactor consisting of: eight sockets lamp, temperature control, mixing and cooling system. Each of the two lamp sets could be triggered individually or simultaneously via switches, modulating the intensity of the emitted light. The photoreactor can operate at three different wavelengths UV-A (320-400 nm), UV-B (280-320 nm), UV-C (200-280 nm, λmax 254 nm).

elements included in the photoreactor:
cooling system
temperature control
mixing system
test tube racks
quartz tube
8 x UV-C lamps
(*Osram, Puritec, HNS, S 9W*)

The detailed plan for the construction of photoreactor see ref.[1]

3. Photochemical reaction in flow.

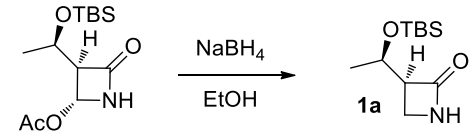
Flow photochemical reactions were performed in a closed system under an argon atmosphere in self-made flow set consisting of: Rayonet-type, self-made photoreactor (*with four UV-C lamps*), UV-transparent FEP tubing of dimensions 0.7 mm i.d. × 1.1 mm o.d, wound on a quartz tube of dimensions 18 cm in length and 4 cm in diameter (*loop length 14 m, capacity 7 mL, number of coils 111*), column (*syringe 1mL*) packed with Celite® 545 (*CAS 68855-54-9*), fluid matering lab pump (*model RP-SY*), magnetic stirrer.



UV-transparent FEP tubing and column packed with Celite.

4. Synthesis of lactams 1a-i.

Lactam **1** was obtained according to the literature procedure.[2]

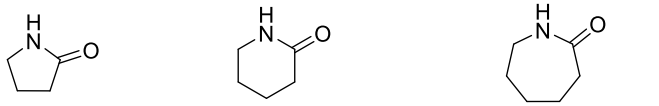


5 g
CAS 76855-69-1

2.901 g

(*S*)-3-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)ethyl)azetidin-2-one; 73%; white solid; $[\alpha]^{D}_{17}$ = – 84.9 (*c* = 0.26); ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.61 (s, 1H), 4.22 (qd, *J* = 6.3, 4.5 Hz, 1H), 3.35 (dd, *J* = 5.0, 2.7 Hz, 1H), 3.29 (t, *J* = 5.2 Hz, 1H), 3.25 – 3.21 (m, 1H), 1.20 (d, *J* = 6.2 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 6H).

Lactam **1b**, **1c** and **1d** are commercially available, and were bought form Sigma Aldrich.



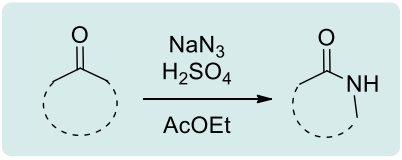
2-Pyrrolidinone (**1b**)
CAS 616-45-5

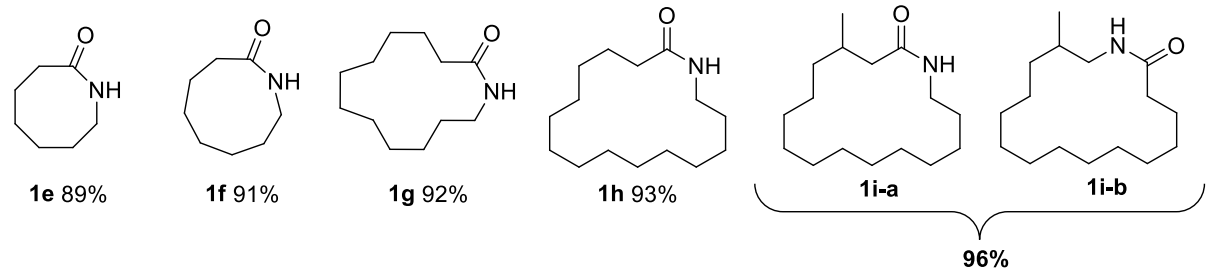
δ-Valerolactam (**1c**)
CAS 675-20-7

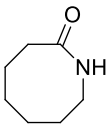
ε-Caprolactam (**1d**)
CAS 105-60-2

4.1 Synthesis of lactams 1e-i *via* Schmidt reaction.

General procedure: To a three-necked round-bottomed flask fitted with a reflux condenser cyclic ketone (4.55 mmol), sodium azide (532 mg, 8.19 mmol, 1.8 equiv.) and ethyl acetate (6 mL) were added. The mixture was stirred at 50 °C for 30 min, then concentrated sulfuric acid (756 µL g, 14.1 mol, 3.1 equiv.) was added dropwise. The reaction mixture was refluxed for 2 h, cooled to room temperature and neutralised with 20% aq. solution of NaOH. After phase separation, the aqua layer was washed with AcOEt. The combined organic layers were washed with H_2O and sat. aq. solution of brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was purified by crystallization or column chromatography.

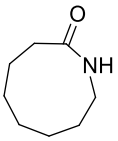






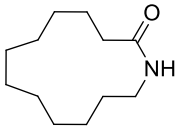
1e

Azocan-2-one; 89% (1.747 g obtained from 2.0 mL of cycloheptanone); purified by column chromatography (1:1 acetone in hexanes); yellow waxy solid; ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.92 (bs, 1H), 3.34 – 3.29 (m, 2H), 2.43 – 2.39 (m, 2H), 1.83 – 1.77 (m, 2H), 1.64 – 1.53 (m, 6H); spectroscopic data are in agreement with literature data.[3]



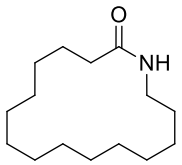
1f

Azonan-2-one; 91% (3.038 g obtained from 3.0 g of cyclooctanone) purified by column chromatography (1:1 acetone in hexanes); white solid; m.p. 76-77 °C; ^{1}H NMR (500 MHz, chloroform-*d*) δ 5.81 (bs, 1H), 3.37 – 3.33 (m, 2H), 2.44 – 2.41 (m, 2H), 1.85 – 1.80 (m, 2H), 1.64 – 1.59 (m, 6H), 1.55 – 1.52 (m, 2H); spectroscopic data are in agreement with literature data.[4]



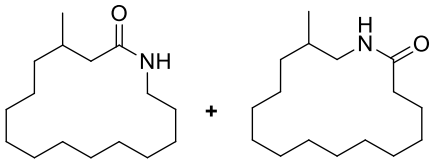
1g

Azacyclotridecan-2-one; 92% (3.973 g; obtained from 4.0 g of cyclododecanone); purified by crystallization from hexanes; white solid; m.p. 150 °C; ^{1}H NMR (500 MHz, chloroform-*d*) δ 5.47 (bs, 1H), 3.33 – 3.28 (m, 2H), 2.21 – 2.18 (m, 2H), 1.71 – 1.65 (m, 2H), 1.54 – 1.49 (m, 2H), 1.40 – 1.27 (m, 14H); spectroscopic data are in agreement with literature data.[5]



1h

Azacyclohexadecan-2-one; 93% (1.016 g, obtained form 1.021 g of cyclopentadecanone); purified by crystallization from hexanes; white solid; m.p. 134 °C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.39 (bs, 1H), 3.35 – 3.30 (m, 2H), 2.20 – 2.16 (m, 2H), 1.69 – 1.61 (m, 2H), 1.52 – 1.45 (m, 2H), 1.36 – 1.25 (m, 20H); spectroscopic data are in agreement with literature data.[6]



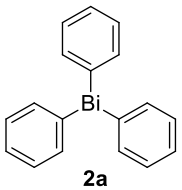
1i-a + **1i-b**

4-Methylazacyclohexadecan-2-one (1i-a) and **15-Methylazacyclohexadecan-2-one (1i-b)**; 96%; (1.024 g, obtained from 1.0 g of muscone CAS 541-91-300); inseparable mixture of isomers in ratio 1.0:1.2; waxy yellow solid; **1i-a** selected signals: ^{1}H NMR (600 MHz, chloroform-*d*) δ 5.71 (bs, 1H), 3.58 (dtd, *J* = 13.7, 7.7, 4.2 Hz, 1H), 2.25 (dd, *J* = 13.5, 3.9 Hz, 1H), 2.00 – 1.93 (m, 1H), 1.84 (dd, *J* = 13.5, 10.5 Hz, 1H), 0.92 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 172.8, 45.3, 39.2, 20.3; **1i-b** selected signals: ^{1}H NMR (600 MHz, chloroform-*d*) δ 5.75 (s, 1H), 3.27 (ddd, *J* = 13.4, 5.4, 3.8 Hz, 1H), 2.17 (td, *J* = 6.4, 3.4 Hz, 2H), 0.87 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 173.2, 45.5, 17.7; HRMS (ESI-TOF) m/z calc for $C_{16}H_{32}NO$ [M+H^{+}] 254.2484. Found 254.2491; IR (film, CH_2Cl_2) *v*: 3289,2927, 2856, 1641, 1554, 1460, 1442, 1376, 1246, 722 cm^{-1}.

5. Synthesis of triarylbismuth compound 2a-l:

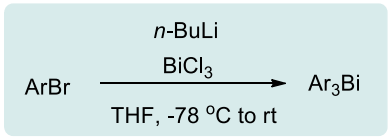
5.1 With organolithium reagent (Method A)

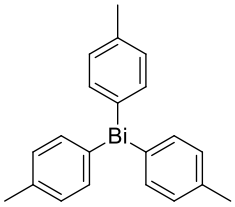
General procedure: Aryl bromide (10.0 mmol) was dissolved in dry THF (30 mL) and cooled to –78 °C. *n*-Butyllithium (4.0 mL 10.0 mmol)(2.5 M in hexanes) was added dropwise under argone. After stirring for 2 h at -78 °C, bismuth(III) chloride (993 mg, 3.15 mmol) dissolved in THF (10 mL) was added dropwise. The mixture was stirred for 30 min, then allowed to warm up to room temperature, and left overnight. The resulting precipitate was filtered through a pad of celite, and washed several time with dichloromethane. The combined filtrates were evaporated under diminished pressure to give a crude product, which was purified by crystallization from hot MeOH to afford pure aryl bismuth compound.



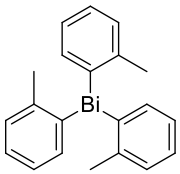
2a

Triphenylbismuth; commercially available; CAS 603-33-8; bought from Sigma Aldrich.

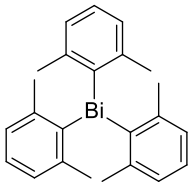




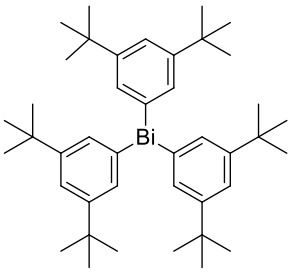
2b 52%



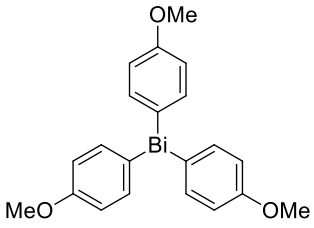
2c 44%



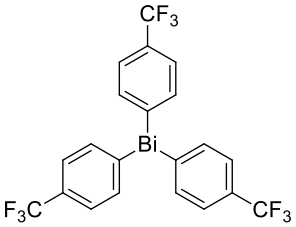
2d 78%



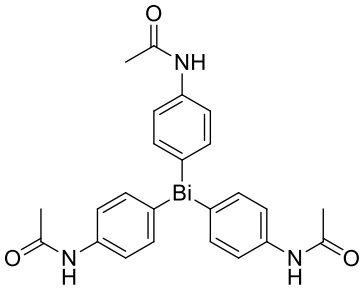
2e 52%



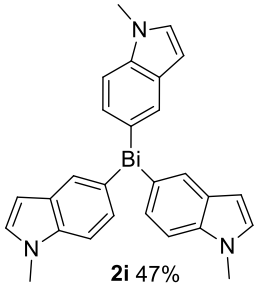
2f 42%



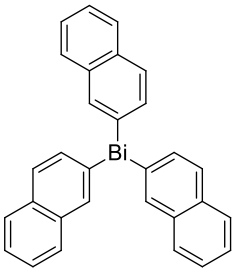
2g 66%



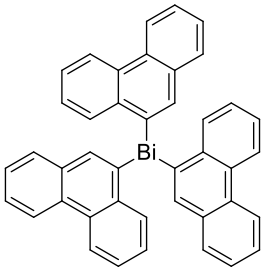
2h 68%



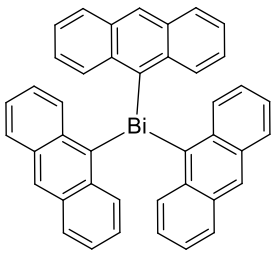
2i 47%



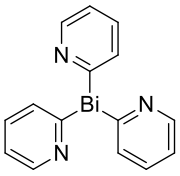
2j 60%



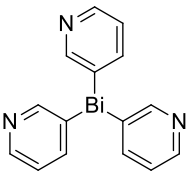
2k 58%



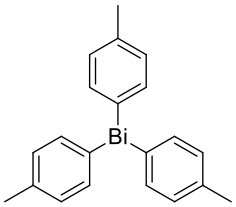
0%



0%

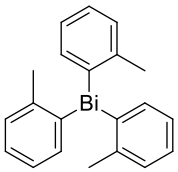


0%



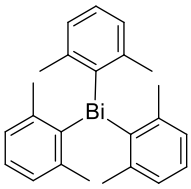
2b

Tri-*p*-tolylbismuth; 52% (936 mg; starting from 2.0 g of 1-bromo-4-methylbenzene); white solid; m.p. 119-120 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 – 7.56 (m, 6H), 7.20 – 7.16 (m, 6H), 2.25 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 152.4, 137.2, 136.6, 131.0, 21.0; spectroscopic data are in agreement with literature data.[7]



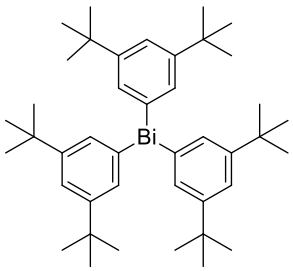
2c

Tri-*o*-tolylbismuth; 44% (781 mg; starting from 1.4 mL of 1-bromo-2-methylbenzene); white solid; m.p. 130-131 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.44 (dd, *J* = 7.4, 1.4 Hz, 3H), 7.37 (dd, *J* = 7.8, 1.4 Hz, 3H), 7.28 (td, *J* = 7.4, 1.4 Hz, 3H), 7.08 (td, *J* = 7.4, 1.4 Hz, 3H), 2.38 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 155.1, 143.8, 138.3, 130.5, 129.0, 128.7, 26.3; spectroscopic data are in agreement with literature data.[7]



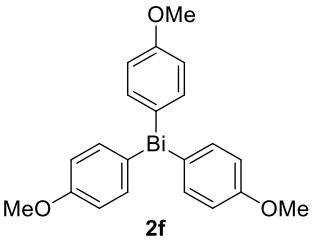
2d

Tri(2,6-dimethylphenyl)bismuth; 51%; (910 mg; starting from 2.0 g of 2-bromo-1,3-dimethylbenzene); slightly yellow solid; m.p. 142-143 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.16 – 7.06 (m, 9H), 2.26 (s, 18H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.5, 145.7, 128.6, 128.3, 27.9.



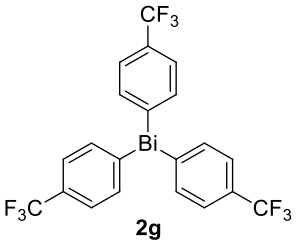
2e

Tris(3,5-di-*tert*-butylphenyl)bismuth; 52% (370 mg; starting from 772 of 1-bromo-3,5-di-tert-butylbenzene); white solid; m.p. 145-146 °C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.54 – 7.52 (m, 6H), 7.34 – 7.32 (m, 3H), 1.21 (s, 54H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 155.3, 152.3, 131.8, 121.6, 35.1, 31.6; spectroscopic data are in agreement with literature data.[8]



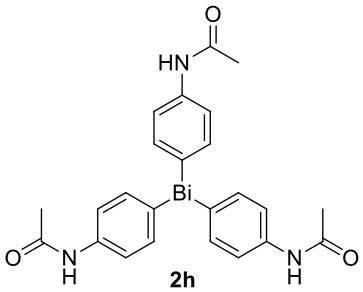
2f

Tris(4-methoxyphenyl)bismuth; 42% (1.187 g; starting from 2.0 mL of 1-bromo-4-methoxybenzene); gray solid; m.p. 192-193 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.59 – 7.55 (m, 6H), 6.96 – 6.91 (m, 6H), 3.72 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.8, 146.1, 138.4, 116.2, 54.8; spectroscopic data are in agreement with literature data.[8]



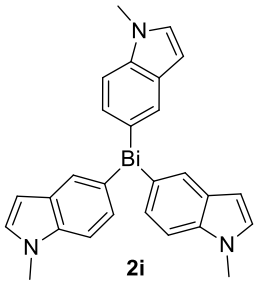
2g

Tris(4-(trifluoromethyl)phenyl)bismuth; 66% (603 mg; starting from 1.0 g of 1-bromo-4-(trifluoromethyl)benzene); slightly yellow solid; m.p. 145-146 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 – 7.89 (m, 6H), 7.71 – 7.67 (m, 6H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.1, 137.9, 130.8 (q, *J* = 32.4 Hz), 127.5 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 272.3 Hz); spectroscopic data are in agreement with literature data.[9]



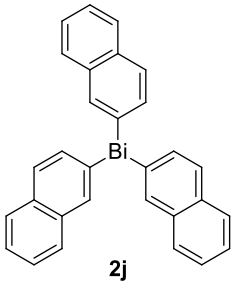
2h

***N*,*N*',*N*''-(Bismuthanetriyltris(benzene-4,1-diyl))triacetamide**; 68% (995 mg; starting from 2.0 g of *N*-(4-bromophenyl)acetamide); slightly yellow solid; m.p. 158-159 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54 (d, *J* = 8.9 Hz, 6H), 7.42 (d, *J* = 8.9 Hz, 6H), 2.01 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.4, 138.9, 131.4, 120.9, 114.3, 24.0.



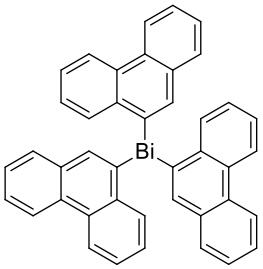
2i

Tris(1-methyl-1*H*-indol-5-yl)bismuth; 47% (318 mg; starting form 750 mg of 5-bromo-1-methyl-1*H*-indole); slightly yellow solid; m.p. 224-225 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.94 (s, 3H), 7.48 (d, J = 8.2 Hz, 3H), 7.42 (d, J = 8.2 Hz, 3H), 7.25 (d, J = 3.1 Hz, 3H), 6.31 (d, J = 3.1 Hz, 3H), 3.74 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 143.9, 135.9, 130.7, 129.8, 129.5, 129.3, 111.7, 100.0, 32.3.



2j

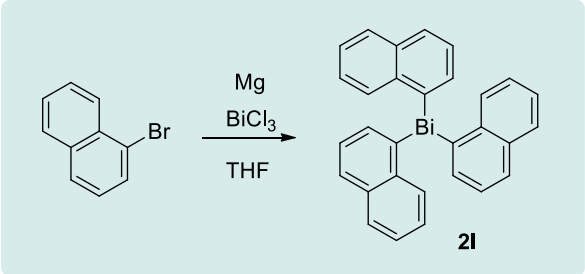
Tri(naphthalen-2-yl)bismuth; 60% (1.086 g; starting from 2.0 g of 2-bromonaphthalene); slightly yellow solid; m.p. 228-229 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (s, 3H), 7.92 – 7.85 (m, 9H), 7.79 – 7.76 (m, 3H), 7.51 – 7.48 (m, 6H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 155.9, 137.7, 135.4, 134.9, 132.8, 129.7, 128.3, 127.9, 126.6, 126.5.



2k

Tri(phenanthren-9-yl)bismuthane; 58% (1.056 g; starting from 2.0 g of 9-bromophenanthrene); the product was additionally recrystallized from toluene; slightly yellow solid; m.p. 287-288 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.92 (d, J = 8.2 Hz, 3H), 8.79 (d, J = 8.3 Hz, 3H), 8.42 (s, 3H), 8.30 (d, J = 8.1 Hz, 3H), 7.67 (t, J = 7.6 Hz, 3H), 7.61 (t, J = 7.6 Hz, 3H), 7.56 (t, J = 7.5 Hz, 3H), 7.43 (t, J = 7.4 Hz, 3H), 7.30 (d, J = 7.9 Hz, 3H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 155.7, 138.9, 136.1, 133.5, 131.0, 130.5, 129.6, 128.4, 127.4, 126.6, 126.5, 126.3, 123.2, 122.5.

5.2 With Grignard reagent (Method B):



To a three-necked round-bottomed flask fitted with a reflux condenser magnesium dust (235 mg, 9.7 mmol), dry THF (20 mL) and iodine crystal were added. To this mixture a solution of 1-bromonaphthalene (1.35 mL, 9.7 mmol) in dry THF (10 mL) was added dropwise under argone. The mixture was reflux until the magnesium was completely consumed (discoloration of the solution from brown to light gray was observed). After generating the Grignard reagent, the mixture was cooled to room temperature. Then, a solution of bismuth(III) chloride (967 mg, 3.06 mmol) in dry THF (10 mL) was added, and the reaction was stirred overnight. The resulting precipitate was filtered through a pad of celite, and washed several time with dichloromethane. The combined filtrates were evaporated under diminished pressure to give a crude product, which was purified by crystallization from hot MeOH to afford 965 mg (56%) of tri(naphthalen-1-yl)bismuth as a slightly yellow solid. m.p. 235-236 °C; ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.14 – 8.08 (m, 3H), 7.96 – 7.89 (m, 3H), 7.89 – 7.87 (m, 6H), 7.54 – 7.42 (m, 6H), 7.30 – 7.22 (m, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.4, 138.84, 138.78, 134.9, 131.1, 129.3, 129.1, 128.7, 126.3, 125.9.

6. Synthesis of *N*-aryl lactams 3a-t:

6.1 Synthesis of *N*-aryl lactams 3a-s *via* copper-catalyzed cross-coupling of lactams with triarylbismuth compounds.

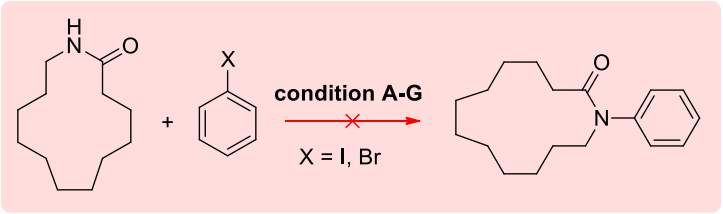
General procedure: N-arylation reactions were performed according to the literature procedure with small modification.[10] The reactions were prepared in glove box. To a sealed tube lactam (0.51 mmol), triarylbismuth compound (1.1-1.2 equiv.), cupric acetate (92 mg, 0.51 mmol, 1.0 eqiuv.), suitable solvent (*see for the individual compounds*), and triethylamine (72 µL, 0.51 mmol, 1.0 equiv.) were added respectively under nitrogen. The reaction mixture was stirred at set temperature for given time. *(Small- and medium- size*

lactams react fast at room temperature. The reaction was stooped after complete conversion of substrate. Large-size lactams requires long heating. The reaction was stopped 24 hours after no progress was observed.) The progress of the reaction was monitored by TLC as well as by the color change from the initial deep blue to turquoise green, with the concomitant precipitation of grayish Cu(I) salt. After the required time, the mixture was filtered through a pad of celite, and washed several time with dichloromethane. The combined filtrates were evaporated under diminished pressure to give a residue, which was preabsorbed onto silica gel, and then purified by flash chromatography.

start of the reaction

complete of the reaction

6.2 The strategies that cannot be used for the synthesis of large-ring N-aryl lactams:



(A)[11] X = I, CuI (5 mol%), CsF (2.0 equiv.), DMEDA (10 mol%), AcOEt, 50 °C.

(B) X = I, CuI (10 mol%), Cs_2CO_3 (1.5 equiv.), DMEDA (20 mol%), toluene, 80 °C.

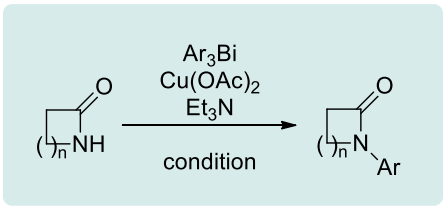
(C)[12] X = I, CuI (5 mol%), K_3PO_4 (2.5 equiv.), glycine (20 mol%), 1,4-dioxane, b.p.

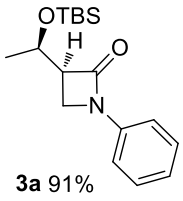
(D)[13] X=I, CuI (5 mol%), K_3PO_4 (2.0 equiv.), DMEDA (10 mol%), 1,4-dioxane, b.p.

(E)[14] X = Br, $Pd_2(dba)_3$ (1 mol%), Xantphos (1.5 mol%), Cs_2CO_3, (1.4 equiv.), 1,4-dioxane, b.p.

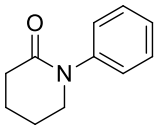
(F) [15] X = Br, $Co(acac)_2$ (10 mol%), CuI (10 mol%), Cs_2CO_3 (2.0 equiv.), NMP, b.p.

(G)[16] X= Br, $Ni(acac)_2$ (10 mol%), CuI (10 mol%), Cs_2CO_3 (2.0 equiv.), NMP, b.p.

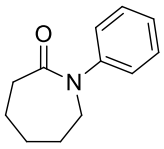




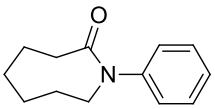
3a 91%



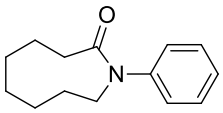
3c 82%



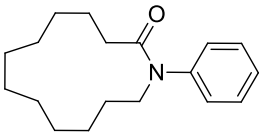
3d 70%



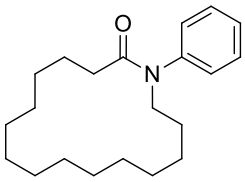
3e 63%



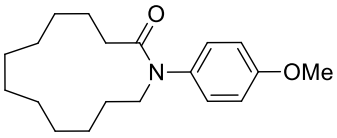
3f 68%



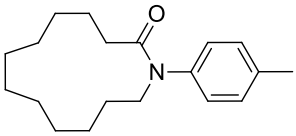
3g 63%



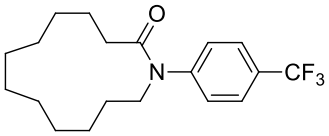
3h 53%



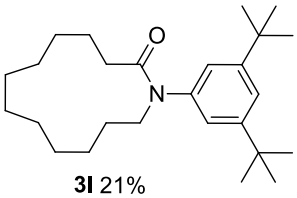
3i 68%



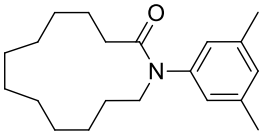
3j 53%



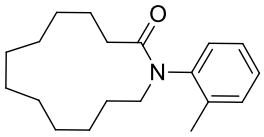
3k 44%



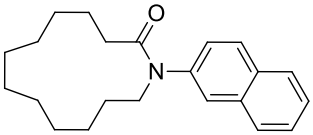
3l 21%



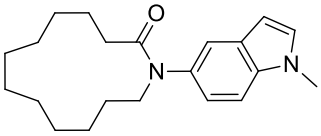
3m 55%



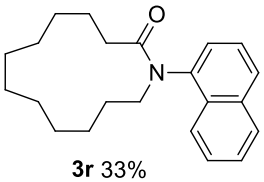
3n 29%



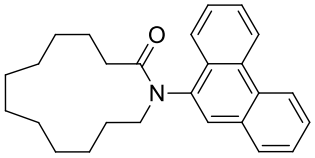
3o 34%



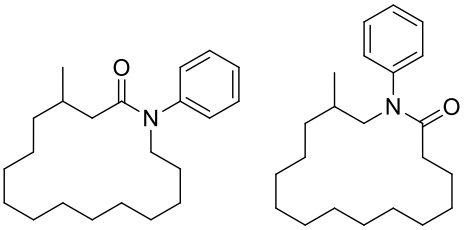
3p 47%



3r 33%

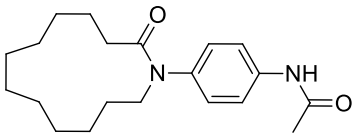


3s 50%

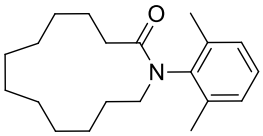


3t-a **1.0 : 1.1** **3t-b**

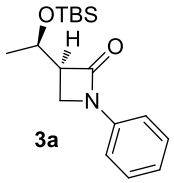
60%



0%

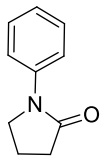


0%



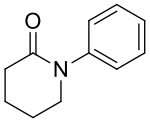
3a

(*S*)-3-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)ethyl)-1-phenylazetidin-2-one; 91% (121 mg; starting from 100 mg of **1a** and 211 mg (1.1 equiv.) of **2a**); reaction was performed in dichloromethane (4 mL) at room temperature for 24 h; yellow solid; R*f* 0.78 (1:3 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.37 – 7.28 (m, 4H), 7.14 – 7.02 (m, 1H), 4.31 (qd, J = 6.2, 4.1 Hz, 1H), 3.67 (dd, J = 5.3, 2.8 Hz, 1H), 3.60 (dd, J = 5.4 Hz, 1H), 3.28 (ddd, J = 5.5, 4.1, 2.8 Hz, 1H), 1.25 (d, J = 6.2 Hz, 3H), 0.79 (s, 8H), 0.07 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 165.6, 138.5, 129.0, 123.6, 116.2, 65.2, 56.6, 40.2, 25.6, 22.6, 17.8, -4.3, -5.0; HRMS (ESI-TOF) m/z calc for $C_{17}H_{27}NO_2NaSi$ [M+Na$^+$] 328.1713. Found 328.1709; IR (film, CH_2Cl_2) *v*: 2954, 2929, 2890, 2856, 1751, 1600, 1501, 1470, 1386, 1257, 1145, 1079, 838, 777, 753, 691 cm^{-1}.



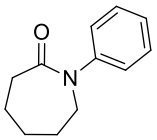
3b

1-Phenyl-2-pyrrolidinone; commercially available; CAS 4641-57-0; bought from Sigma Aldrich.



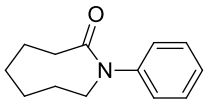
3c

1-Phenylpiperidin-2-one; 82% (144 mg; starting from 100 mg of **1c** and 211 mg (1.1 equiv.) of **2a**); reaction was performed in dichloromethane (4 mL) at room temperature for 24 h; yellow solid; m.p. 100-101 °C; R*f* 0.33 (1:3 acetone in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.43 – 7.34 (m, 2H), 7.31 – 7.20 (m, 3H), 3.68 – 3.62 (m, 2H), 2.60 – 2.52 (m, 2H), 1.98 – 1.90 (m, 4H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 170.1, 143.6, 129.3, 126.8, 126.4, 51.8, 33.0, 23.7, 21.6; HRMS (ESI-TOF) m/z calc for $C_{11}H_{14}NO$ [M+H$^+$] 176.1075. Found 176.1079; IR (film, CH_2Cl_2) *v*: 2959, 1641, 1594, 1492, 1429, 1347, 1327, 1307, 1240, 1179, 1162, 765, 700, 547 cm^{-1};); spectroscopic data are in agreement with literature data.[17]



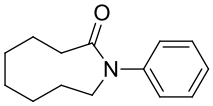
3d

1-Phenylazepan-2-one; 70% (117 mg; starting from 100 mg of **1d** and 211 mg (1.1 equiv.) of **2a**); reaction was performed in dichloromethane (4 mL) at room temperature for 24 h; colorless waxy solid; R*f* 0.41 (1:1 acetone in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.40 – 7.34 (m, 2H), 7.25 – 7.19 (m, 3H), 3.78 – 3.73 (m, 2H), 2.73 – 2.67 (m, 2H), 1.86 – 1.78 (m, 6H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 175.6, 144.7, 129.2, 126.5, 126.4, 53.1, 37.8, 30.0, 29.1, 23.7; HRMS (ESI-TOF) m/z calc for $C_{12}H_{16}NO$ [M+H^{+}] 190.1232. Found 190.1236; IR (film, CH_2Cl_2) *v*: 2928, 1658, 1594, 1494, 1442, 1409, 1351, 1216, 1198, 1150, 1124, 1078, 982, 761, 697, 591, 550 cm^{-1}; spectroscopic data are in agreement with literature data.[18]



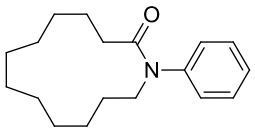
3e

1-Phenylazocan-2-one; 63% (101 mg; starting from 100 mg of **1e** and 211 mg (1.1 equiv.) of **2a**); reaction was performed in dichloromethane (3 mL) at room temperature for 24 h; colorless oil; R*f* 0.38 (1:1 acetone in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.41 – 7.36 (m, 2H), 7.28 – 7.20 (m, 3H), 3.85 – 3.81 (m, 2H), 2.70 – 2.66 (m, 2H), 1.96 – 1.90 (m, 2H), 1.73 – 1.61 (m, 6H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.8, 142.7, 129.3, 127.5, 126.9, 50.8, 34.7, 29.6, 29.1, 26.5, 24.8; HRMS (ESI-TOF) m/z calc for $C_{13}H_{18}NO$ [M+H^{+}] 204.1388. Found 204.1390; IR (film, CH_2Cl_2) *v*: 2925, 2858, 649, 1594, 1494, 1452, 1409, 1360, 1253, 1212, 1147, 1125, 756, 697, 591 cm^{-1}.



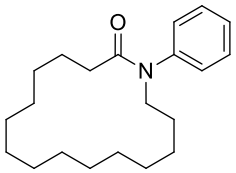
3f

1-Phenylazonan-2-one; 68% (103 mg; starting from 100 mg of **1f** and 211 mg (1.1 equiv.) of **2a**); reaction was performed in dichloromethane (3 mL) at room temperature for 4 days; colorless solid; m.p. 51-52 °C; R*f* 0.47 (1:1 acetone in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.42 – 7.35 (m, 2H), 7.29 – 7.21 (m, 3H), 3.89 – 3.84 (m, 2H), 2.70 – 2.64 (m, 1H), 1.98 – 1.90 (m, 2H), 1.79 – 1.71 (m, 2H), 1.69 (d, J = 14.7 Hz, 2H), 1.65 – 1.57 (m, 4H); ^{13}CNMR (126 MHz, chloroform-*d*) δ 175.2, 142.8, 129.3, 127.6, 127.0, 52.3, 35.3, 28.3, 27.4, 26.1, 24.8, 22.3; HRMS (ESI-TOF) m/z calc for $C_{14}H_{20}NO$ [M+H^{+}] 218.1545. Found 218.1548; IR (film, CH_2Cl_2) *v*: 3464, 2925, 2881, 1643, 1594, 1493, 1451, 1493, 1409, 1353, 1191, 1024, 63, 697, 585 cm^{-1}.



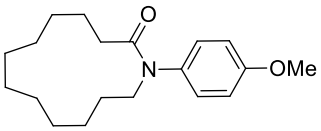
3g

1-Phenylazacyclotridecan-2-one; 63% (130 mg; starting from 150 mg of **1g** and 368 mg (1.1 equiv.) of **2a**); reaction was performed in mixture of dichloromethane (4 mL) and 1,4-dioxane (4 mL) at 80 °C for 4 days; white solid; m.p. 124-125 °C; R*f* 0.35 (1:4 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.45 – 7.39 (m, 2H), 7.37 – 7.31 (m, 1H), 7.24 – 7.18 (m, 2H), 4.82 – 4.60 (m, 1H), 2.86 – 2.71 (m, 1H), 2.20 – 2.08 (m, 1H), 2.04 – 1.89 (m, 0H), 1.82 – 1.68 (m, 3H), 1.57 – 1.21 (m, 16H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.1, 144.0, 129.7, 128.6, 127.7, 48.9, 34.5, 27.2, 26.9, 26.6, 26.0, 25.9, 25.4, 25.2, 25.1, 24.4.; HRMS (ESI-TOF) m/z calc for $C_{18}H_{28}NO$ [M+H^{+}] 274.2171. Found 274.2177; IR (film, CH_2Cl_2) *v*: 2926, 2859, 1643, 1594, 1493, 1453, 1400, 1356, 1266, 1177, 1100, 773, 742, 708, 561 cm^{-1}.



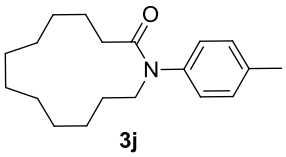
3h

1-Phenylazacyclohexadecan-2-one; 53% (87 mg; starting from 125 mg of **1h** and 253 mg (1.1 equiv.) of **2a**); reaction was performed in mixture of dichloromethane (3 mL) and 1,4-dioxane (3 mL) at 100 °C for 3 days; white solid; m.p. 75-76 °C; R*f* 0.51 (1:4 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.46 – 7.38 (m, 2H), 7.38 – 7.31 (m, 1H), 7.18 – 7.10 (m, 2H), 3.84 – 3.76 (m, 2H), 2.05 – 2.00 (m, 2H), 1.62 – 1.26 (m, 24H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 203.0, 151.5, 134.7, 131.9, 117.8, 113.6, 111.9, 41.9, 38.3, 28.6, 28.4, 28.3, 28.1, 27.70, 27.65, 27.3, 27.2, 26.5, 25.7, 24.0; HRMS (ESI-TOF) m/z calc for $C_{21}H_{34}NO$ [M+H^{+}] 316.2640. Found 316.2644; IR (film, CH_2Cl_2) *v*: 2925, 2855, 1657, 1595, 1495, 1457, 1398, 1269, 772, 701, 563 cm^{-1}.



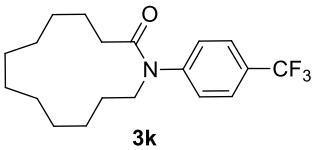
3i

1-(4-Methoxyphenyl)azacyclotridecan-2-one; 68% (103 mg; starting from 100 mg of **1g** and 296 mg (1.1 equiv.) of **2f**); reaction was performed in mixture of dichloromethane (4 mL) and 1,4-dioxane (4 mL) at 100 °C for 2 days; colorless oil; R*f* 0.35 (1:4 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.13 – 7.11 (m, 2H), 6.94 – 6.89 (m, 2H), 4.75 – 4.68 (m, 1H), 3.83 (s, 3H), 2.77 – 2.70 (m, 1H), 2.19 – 2.13 (m, 1H), 1.96 – 1.90 (m, 1H), 1.75 – 1.65 (m, 2H), 1.55 – 1.21 (m, 16H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.4, 158.9, 136.6, 129.6, 114.8, 55.6, 48.7, 34.3, 27.2, 26.9, 26.5, 26.03, 25.99, 25.4, 25.1, 25.0, 24.3; HRMS (ESI-TOF) m/z calc for $C_{19}H_{30}NO_2$ [M+H^{+}] 304.227. Found 304.2284; IR (film, CH_2Cl_2) *v*: 2927, 2858, 1652, 1511, 1443, 1397, 1248, 1178, 1105, 104, 835, 563 cm^{-1}.



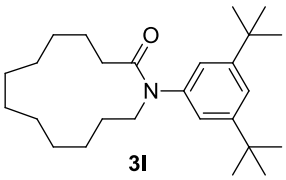
3j

1-(*p*-Tolyl)azacyclotridecan-2-one; **1-(4-Methoxyphenyl)azacyclotridecan-2-one**; 53% (78 mg; starting from 100 mg of **1g** and 295 mg (1.1 equiv.) of **1b**); reaction was performed in mixture of dichloromethane (4 mL) and 1,4-dioxane (4 mL) at 100 °C for 2 days; white solid; m.p. 66-67 °C; R*f* 0.71 (1:2 acetone in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.22 – 7.17 (m, 2H), 7.10 – 7.05 (m, 2H), 4.75 – 4.67 (m, 1H), 2.78 – 2.70 (m, 1H), 2.37 (s, 3H), 2.20 – 2.11 (m, 1H), 1.97 – 1.89 (m, 1H), 1.75 – 1.63 (m, 2H), 1.55 – 1.20 (m, 16H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.2, 141.2, 137.6, 130.3, 128.3, 48.7, 34.3, 27.1, 26.9, 26.5, 25.93, 25.88, 25.3, 25.1, 24.9, 24.3, 21.2; HRMS (ESI-TOF) m/z calc for $C_{19}H_{30}NO$ [M+H^{+}] 288.2327. Found 288.2332; IR (film, CH_2Cl_2) *v*: 2926, 2859, 1656,1513, 1445, 1395, 1280, 822, 560 cm^{-1}.



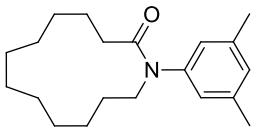
3k

1-(4-(Trifluoromethyl)phenyl)azacyclotridecan-2-one; 44% (76 mg; starting from 100 mg of **1g** and 361 mg (1.1 equiv.) of **2g**); reaction was performed in mixture of dichloromethane (4 mL) and 1,4-dioxane (4 mL) at 100 °C for 2 days; waxy solid; R*f* 0.19 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.70 – 7.65 (m, 2H), 7.36 – 7.31 (m, 2H), 4.84 – 4.61 (m, 1H), 2.90 – 2.70 (m, 1H), 2.19 – 1.95 (m, 2H), 1.84 – 1.65 (m, 2H), 1.56 – 1.14 (m, 16H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 173.8, 147.2, 129.7, 128.7, 126.8, 123.9 (q, J = 272.4 Hz), 49.2, 34.5, 29.8, 27.0, 26.7, 26.4, 26.0, 25.4, 25.3, 25.1, 24.2.; HRMS (ESI-TOF) m/z calc for $C_{19}H_{27}NOF_3$ [M+H^{+}] 342.2045. Found 342.2053; IR (film, CH_2Cl_2) *v*: 2930, 2861, 1662, 1612, 1393, 1326, 1167, 1128, 1067, 1016, 847 cm^{-1}.



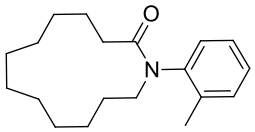
3l

1-(3,5-di-*tert*-Butylphenyl)azacyclotridecan-2-one; 21% (31 mg; starting from 75 mg of **1g** and 356 mg (1.2 equiv.) of **2e**); reaction was performed in mixture of dichloromethane (4 mL) and 1,4-dioxane (4 mL) at 100 °C for 3 days; white solid; m.p. 143-144 °C; R*f* 0.29 (1:9 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.37 (s, 1H), 7.05 (s, 2H), 4.77 – 4.67 (m, 1H), 2.83 – 2.75 (m, 1H), 2.20 – 2.11 (m, 1H), 1.97 – 1.90 (m, 1H), 1.77 – 1.63 (m, 2H), 1.54 – 1.42 (m, 6H), 1.38 – 1.29 (m, 28H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.2, 152.4, 143.0, 122.9, 121.4, 48.6, 35.1, 34.4, 31.5, 29.8, 27.2, 27.1, 26.9, 25.9, 25.8, 25.4, 25.3, 25.0, 24.2; HRMS (ESI-TOF) m/z calc for $C_{26}H_{44}NO$ [M+H^{+}] 386.3423. Found 386.3426; IR (film, CH_2Cl_2) *v*: 2959, 2926, 2861, 1654, 1593, 1441, 1393, 1362, 127, 736, 716 cm^{-1}.



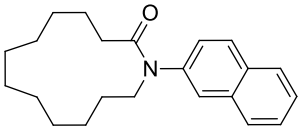
3m

1-(3,5-Dimethylphenyl)azacyclotridecan-2-one; 55% (85 mg; starting from 100 mg of **1g** and 321 mg (1.2 equiv.) of **2d**); reaction was performed in toluene (8 mL) at 120 °C for 1 days; slightly yellow solid; m.p. 120-121 °C; R*f* 0.34 (1:9 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 6.96 (s, 1H), 6.80 (s, 2H), 4.74 – 4.64 (m, 1H), 2.78 – 2.72 (m, 1H), 2.33 (s, 6H), 2.21 – 2.14 (m, 1H), 1.98 – 1.91 (m, 1H), 1.80 – 1.65 (m, 2H), 1.56 – 1.25 (m, 16H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.2, 139.4, 135.3, 129.3, 126.1, 48.8, 34.4, 27.2, 27.0, 26.6, 26.1, 25.9, 25.4, 25.2, 25.1, 24.4, 21.4; HRMS (ESI-TOF) m/z calc for $C_{20}H_{32}NO$ [M+H^{+}] 302.2484. Found 302.2488; IR (film, CH_2Cl_2) *v*: 2925, 2858, 1654, 1606, 1445, 1395, 1354, 1299, 1233, 1194, 1041, 852, 742, 710 cm^{-1}.



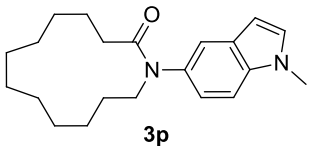
3n

1-(*o*-Tolyl)azacyclotridecan-2-one; 29% (43 mg; starting from 100 mg of **1g** and 295 mg (1.2 equiv.) of **2c**); reaction was performed in toluene (8 mL) at 120 °C for 3 days; waxy solid; R*f* 0.17 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.29 – 7.24 (m, 4H), 4.76 – 4.65 (m, 1H), 2.63 – 2.56 (m, 1H), 2.17 (s, 3H), 2.06 – 2.00 (m, 1H), 1.92 – 1.83 (m, 1H), 1.75 – 1.61 (m, 2H), 1.56 – 1.27 (m, 16H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 174.2, 142.2, 136.4, 131.7, 129.5, 128.2, 126.8, 46.9, 33.8, 27.2, 27.1, 26.7, 26.0, 25.7, 25.3, 25.0, 24.7, 24.2, 17.6; HRMS (ESI-TOF) m/z calc for $C_{19}H_{30}NO$ [M+H^{+}] 288.2327. Found 288.2326; IR (film, CH_2Cl_2) *v*: 2926, 2857, 1649, 1600, 1491, 1442, 1307, 1356, 1281, 1264, 1095, 772, 732 cm^{-1}.



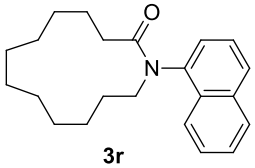
3o

1-(Naphthalen-2-yl)azacyclotridecan-2-one; 34% (104 mg; starting from 185 mg of **1g** and 665 mg (1.2 equiv.) of **2j**); reaction was performed in mixture of dichloromethane (6 mL) and 1,4-dioxane (6 mL) at 100 °C for 4 days; colorless oil; R*f* 0.17 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.91 – 7.84 (m, 3H), 7.70 – 7.66 (m, 1H), 7.56 – 7.51 (m, 2H), 7.34 – 7.30 (m, 1H), 4.85 – 4.76 (m, 1H), 2.95 – 2.84 (m, 1H), 2.24 – 2.16 (m, 1H), 2.05 – 1.97 (m, 1H), 1.82 – 1.70 (m, 2H), 1.56 – 1.30 (m, 16H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.3, 141.3, 133.8, 132.5, 129.8, 128.1, 127.8, 126.9, 126.9, 126.8, 126.7, 49.0, 34.7, 27.2, 27.0, 26.6, 26.1, 25.9, 25.5, 25.2, 25.1, 24.5; HRMS (ESI-TOF) m/z calc for $C_{22}H_{30}NO$ [M+H^{+}] 324.2327. Found 324.2325; IR (film, CH_2Cl_2) *v*: 3056, 2927, 2858, 1656, 1597, 1505, 1444, 1396, 1352, 1276, 1234, 859, 817, 749, 481 cm^{-1}.



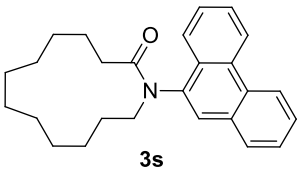
3p

1-(1-Methyl-1*H*-indol-5-yl)azacyclotridecan-2-one; 47% (130 mg; starting from 87.4 mg of **1g** and 292 mg (1.1 equiv.) of **2i**); reaction was performed in toluene (5 mL) at 120 °C for 1 days; pink solid; m.p. 99-100 °C; R*f* 0.28 (1:4 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.45 (s, 1H), 7.33 (d, J = 8.5 Hz, 1H), 7.12 (d, J = 3.1 Hz, 1H), 7.08 – 7.02 (m, 1H), 6.52 (d, J = 3.1 Hz, 1H), 4.83 – 4.75 (m, 1H), 3.82 (s, 3H), 2.86 – 2.80 (m, 1H), 2.20 (ddd, J = 12.9, 9.8, 2.5 Hz, 1H), 1.96 – 1.90 (m, 1H), 1.74 – 1.66 (m, 2H), 1.60 – 1.27 (m, 16H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.8, 136.0, 135.8, 130.3, 129.0, 122.2, 120.6, 110.1, 101.5, 49.0, 34.4, 33.2, 27.3, 27.0, 26.6, 26.1, 26.0, 25.5, 25.2, 25.0, 24.4; HRMS (ESI-TOF) m/z calc for $C_{21}H_{31}N_2O$ [M+H$^+$] 327,2436. Found 327.2432; IR (film, CH_2Cl_2) *v*: 3469, 2926, 2858, 1646, 1490, 1445, 1399, 1260, 723 cm^{-1}.



3r

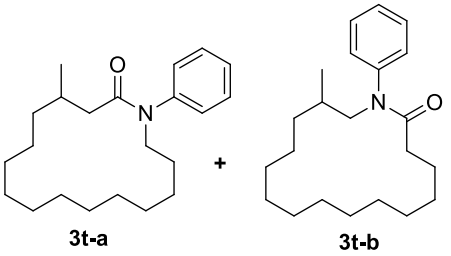
1-(Naphthalen-1-yl)azacyclotridecan-2-one; 33% (55 mg; starting from 100 mg of **1g** and 361 mg (1.2 equiv.) of **2l**); reaction was performed in mixture of dichloromethane (4 mL) and 1,4-dioxane (4 mL) at 100 °C for 3 days; white solid; m.p. 177-178 °C; R*f* 0.38 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.94 – 7.84 (m, 2H), 7.79 – 7.72 (m, 1H), 7.57 – 7.45 (m, 4H), 4.95 – 4.84 (m, 1H), 2.81 – 2.71 (m, 1H), 2.02 – 1.91 (m, 1H), 1.89 – 1.69 (m, 2H), 1.71 – 1.28 (m, 17H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 175.1, 139.5, 135.1, 131.1, 128.7, 128.6, 127.6, 126.8, 126.7, 125.5, 122.7, 47.7, 34.2, 27.7, 27.2, 26.8, 26.2, 25.8, 25.5, 25.3, 24.8, 24.4; HRMS (ESI-TOF) m/z calc for $C_{22}H_{30}NO$ [M+H$^+$] 324.2327. Found 324.2328; IR (film, CH_2Cl_2) *v*: 3057, 2925, 2858, 1649, 1594, 1461, 1442, 1400, 1281, 808, 779 cm^{-1}.



3s

1-(Phenanthren-9-yl)azacyclotridecan-2-one; 50% (95 mg; starting from 100 mg of **1g** and 450 mg (1.2 equiv.) of **2k**); reaction was performed in mixture of toluene (10 mL) and 1,4-dioxane (5 mL) at 120 °C for 4 days; yellow solid; m.p. 165-166 °C; R*f* 0.38 (1:9 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 8.75 (d, J = 8.3 Hz, 1H), 8.71 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 7.75 – 7.70 (m, 3H), 7.68 – 7.63 (m, 2H), 4.95 – 4.87 (m, 1H), 2.82 – 2.77 (m, 1H), 2.13 – 2.08 (m, 1H), 1.92 – 1.85 (m, 1H), 1.81 – 1.74 (m, 1H), 1.68 – 1.34 (m, 17H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 175.2, 137.7, 132.0, 131.3, 130.2, 129.9, 129.2, 127.9, 127.7, 2x127.6, 127.3, 123.5, 123.4, 122.8, 47.4, 34.3, 27.8, 27.3,

26.9, 26.3, 25.7, 25.5, 25.4, 24.8, 24.4; HRMS (ESI-TOF) m/z calc for $C_{26}H_{32}NO$ [M+H$^+$] 374.2484. Found 374.2486; IR (film, CH_2Cl_2) *v*: 2927, 2858, 1656, 1624, 1450, 1394, 1252, 769, 749, 728 cm^{-1}.



3t-a 3t-b

4-Methyl-1-phenylazacyclohexadecan-2-one (3t-a) and **15-Methyl-1-phenylazacyclohexadecan-2-one (3t-b)**; 60%; (233 mg, obtained from 300 mg of mixture **1i-a** and **1i-b** in ratio 1.0:1.2); inseparable mixture of isomers in ratio 1.0:1.1 (**3t-a**:**3t-b**); waxy yellow solid; R*f* 0.33 (1:9 AcOEt in hexanes); **1i-a** selected signals: ^{1}H NMR (600 MHz, chloroform-*d*) δ 4.49 – 4.41 (m, 1H), 3.11 – 3.04 (m, 1H), 1.91 (dd, *J* = 14.8, 3.4 Hz, 1H), 1.84 (dd, *J* = 14.8, 10.7 Hz, 1H), 0.75 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 172.4, 143.1, 42.0, 30.7, 19.9; **1i-b** selected signals: ^{1}H NMR (600 MHz, chloroform-*d*) δ 4.25 (t, *J* = 12.5 Hz, 1H), 2.87 (dd, *J* = 13.4, 3.3 Hz, 1H), 1.96 (dt, *J* = 14.8, 5.1 Hz, 1H), 0.78 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 173.1, 143.3, 54.9, 33.4, 31.7, 17.1; HRMS (ESI-TOF) m/z calc for $C_{22}H_{36}NO$ [M+H$^+$] 330.2797. Found 330.2806; IR (film, CH_2Cl_2) *v*: 2926, 2856, 1659, 1595, 1495, 1458, 1397, 1258, 775, 701, 597 cm^{-1}.

7. Photochemical Fries-type rearrangement of *N*-aryl lactams 3a-t in bath and flow. General procedure for the synthesis of 4a-s.

7.1 Reaction in Bath:

The reaction was prepared in glove box. To the quartz vial containing *N*-aryl lactam **3a-t** (0.1 mmol) degassed MeOH (5 mL) or cyclohexane (5 mL) was added. The vial was sealed with a septum (wrapped with aluminum foil) and transferred to a photoreactor. The reaction was irradiated with eight UV-C lamps (9W, 254 nm) at internal temperature 25-35 °C until complete conversion of substrate (TLC monitoring). After evaporation of the solvent, the residue was preabsorbed onto silica gel, and purified by flash chromatography.

7.2 Reaction in Flow:

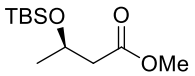
General remarks for flow conditions:

The flow reactions were prepared in glovebox (*weighting the substrate and adding the solvent*). Before every reaction, argon was pumped through the flow set for 15 min. Fluid

matering lab pump flow was set to 10 mL/min. The reactions were irradiated with four UV-C lamps (9W, 254 nm) at internal temperature 25-35 °C.

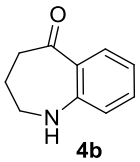
General Procedure in flow:

Substrate **3o-t** (0.1 mmol) was dissolved in 10 mL of degassed cyclohexane in the pear-shaped 25 mL flask equipped with a stirring bar. The flask was connected to the flow set and pumping of the solution was started. After a 5 minutes required to stabilize the flow, UV-C lamps were switched on simultaneously. The progress of the reaction was monitored by TLC. After complete conversion of substrate **3o-t** the reaction was stopped by turning off the lamps. The reaction mixture was collected in a flask, the flow set was rinsed with 10 mL of cyclohexane, both solutions were combined and concentrated. The crude product was preabsorbed onto silica gel, and then purified by column chromatography.



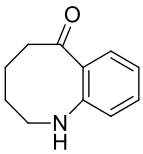
4a

Methyl (*R*)-3-((*tert*-butyldimethylsilyl)oxy)butanoate; 26% (10 mg; starting from 52 mg of **3a**); reaction in bath performed in degassed methanol (9 mL) for 4 h; colorless oil; $[\alpha]_D^{23}$ = – 27.3 (c = 0.98, $CDCl_3$); R*f* 0.28 (1:2 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 4.28 (dq, J = 12.3, 6.0 Hz, 1H), 3.66 (s, 3H), 2.48 (dd, J = 14.5, 7.7 Hz, 1H), 2.38 (dd, J = 14.5, 5.2 Hz, 1H), 1.19 (d, J = 6.1 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H).; spectroscopic data are in agreement with literature data.[19]



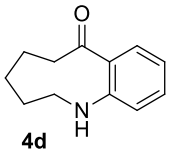
4b

1,2,3,4-tetrahydro-*5H*-benzo[*b*]azepin-5-one; 16% (7 mg; starting from 45 mg of **3b**); reaction in bath performed in degassed methanol (13 mL) for 4 h; white solid; m.p.; 69-70 °C; R*f* 0.69 (1:1 acetone in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.73 (dd, J = 7.9, 1.7 Hz, 1H), 7.25 – 7.22 (m, 1H), 6.83 – 6.80 (m, 1H), 6.74 (dd, J = 8.2, 1.1 Hz, 1H), 4.59 (bs, 1H), 3.25 (t, J = 6.8 Hz, 2H), 2.83 (t, J = 7.2 Hz, 2H), 2.20 – 2.14 (m, 2H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 202.9, 153.7, 132.5, 129.7, 125.5, 118.9, 117.8, 48.1, 41.4, 31.5; spectroscopic data are in agreement with literature data.[20]



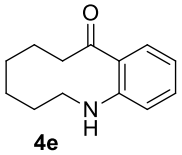
4c

2,3,4,5-Tetrahydrobenzo[*b*]azocin-6(1*H*)-one; 8% (3 mg; starting from 37 mg of **3c**); reaction in bath performed in degassed methanol (10 mL) for 3 h; yellow oil; R*f* 0.72 (1:1 acetone in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.35 (dd, J = 7.7, 1.7 Hz, 1H), 7.23 – 7.18 (m, 1H), 6.76 – 6.72 (m, 1H), 6.63 (dd, J = 8.2, 1.0 Hz, 1H), 4.24 (bs, 1H), 3.19 – 3.15 (m, 2H), 2.81 – 2.76 (m, 2H), 1.98 – 1.91 (m, 2H), 1.80 – 1.72 (m, 2H); spectroscopic data are in agreement with literature data.[21]



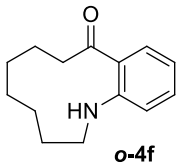
4d

1,2,3,4,5,6-Hexahydro-7*H*-benzo[*b*]azonin-7-one; 32% (12 mg; starting from 38 mg of **3d**); reaction in bath performed in degassed methanol (10 mL) for 3 h; colorless oil; R*f* 0.67 (1:1 acetone in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ δ 7.37 (dd, J = 7.6, 1.7 Hz, 1H), 7.24 – 7.23 (m, 1H), 6.89 (t, J = 7.4 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 3.64 (bs, 1H), 3.14 (t, J = 5.9 Hz, 2H), 2.86 – 2.83 (m, 2H), 1.94 – 1.89 (m, 2H), 1.86 – 1.81 (m, 2H), 1.68 – 1.60 (m, 2H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 209.4, 150.3, 131.7, 131.5, 129.1, 120.3, 119.9, 52.5, 42.0, 29.7, 27.1, 24.9; HRMS (ESI-TOF) m/z calc for $C_{12}H_{16}NO$ [M+H^{+}] 190.1232. Found 190.123; IR (film, CH_2Cl_2) *v*: 3353, 2926, 2857, 1738, 1668, 1600, 1479, 1447, 1327, 1274, 1215, 1032, 756 cm^{-1}.



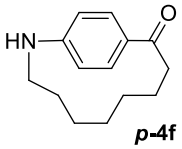
4e

2,3,4,5,6,7-Hexahydrobenzo[*b*]azecin-8(1*H*)-one; 45% (18 mg; starting from 40 mg of **3e**); reaction in bath performed in degassed methanol (10 mL) for 3 h; yellow oil; R*f* 0.47 (1:4 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.34 – 7.29 (m, 1H), 7.27 – 7.25 (m, 1H), 7.03 (d, J = 8.1 Hz, 1H), 6.97 – 6.92 (m, 1H), 4.23 (bs, 1H), 3.11 – 3.07 (m, 2H), 2.93 – 2.89 (m, 2H), 1.74 – 1.69 (m, 2H), 1.50 – 1.46 (m, 4H), 1.31 – 1.25 (m, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 210.5, 146.8, 134.6, 131.8, 127.2, 122.7, 121.5, 49.9, 42.0, 26.4, 25.4, 22.6, 21.1; HRMS (ESI-TOF) m/z calc for $C_{13}H_{18}NO$ [M+H^{+}] 204.1388. Found 204.1389; IR (film, CH_2Cl_2) *v*: 3343, 2931, 2852, 1675, 1600, 1468, 1369, 1279, 1251, 1217, 1158, 758 cm^{-1}.



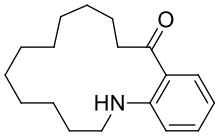
***o*-4f**

1,2,3,4,5,6,7,8-Octahydro-9*H*-benzo[*b*][1]azacycloundecin-9-one; 50% (17 mg; starting from 34 mg of **3f**); reaction in bath in degassed methanol (8 mL) for 3 h; yellow waxy solid; R*f* 0.78 (1:4 AcOEt in hexanes); ^{1}H NMR (600 MHz, chloroform-*d*) δ 7.39 (dd, J = 7.8, 1.6 Hz, 1H), 7.33 – 7.30 (m, 1H), 6.97 (dd, J = 8.3, 1.1 Hz, 1H), 6.80 – 6.74 (m, 1H), 5.97 (bs, 1H), 3.25 – 3.22 (m, 2H), 2.80 – 2.78 (m, 2H), 1.73 – 1.68 (m, 2H), 1.38 – 1.34 (m, 2H), 1.25 (p, J = 6.6 Hz, 2H), 1.16 (p, J = 6.6 Hz, 2H), 1.10 – 1.05 (m, 2H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 209.5, 149.0, 132.6, 130.3, 128.6, 119.1, 118.1, 47.9, 42.6, 28.5, 27.4, 25.2, 24.4, 22.2; HRMS (ESI-TOF) m/z calc for $C_{14}H_{20}NO$ [M+H^{+}] 218.1545. Found 218, 1544; IR (film, CH_2Cl_2) *v*: 3368, 2933, 2867, 1656, 1603, 1571, 1499, 1461, 1446, 1300, 1258, 1205, 1161, 761, 597 cm^{-1}.



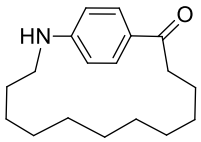
***p*-4f**

2-Aza-1(1,4)-benzenacyclodecaphan-10-one; 30% (11 mg; starting from 34 mg of **3f**); reaction in bath performed in degassed methanol (8 mL) for 3 h; yellow oil; R*f* 0.15 (1:4 AcOEt in hexanes); ^{1}H NMR (600 MHz, chloroform-*d*) δ 7.51 – 7.49 (m, 2H), 6.96 – 6.94 (m, 2H), 3.35 – 3.33 (m, 2H), 2.65 – 2.63 (m, 2H), 1.36 – 1.30 (m, 4H), 0.99 – 0.94 (m, 2H), 0.96 – 0.88 (m, 2H), 0.06 – -0.02 (m, 2H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 205.5, 152.3, 132.0, 129.9, 119.9, 50.5, 44.3, 30.4, 30.1, 29.8, 28.5, 25.6; HRMS (ESI-TOF) m/z calc for $C_{14}H_{20}NO$ [M+H^{+}] 218.1545. Found 218, 1542; IR (film, CH_2Cl_2) *v*: 3335, 2928, 2854, 1669, 1593, 1513, 1462, 1269, 1170, 838, 555 cm^{-1}.



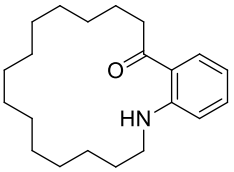
***o*-4g**

1,2,3,4,5,6,7,8,9,10,11,12-Dodecahydro-13*H*-benzo[*b*][1]azacyclopentadecin-13-one; 36% (8 mg; starting from 22 mg of **3g**); reaction in bath performed in degassed methanol (4 mL) for 4 h; yellow oil; R*f* 0.65 (1:4 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 8.65 (bs, 1H), 7.68 (dd, J = 8.1, 1.7 Hz, 1H), 7.32 (dd, J = 8.6 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 6.57 (dd, J = 7.5 Hz, 1H), 3.31 (q, J = 5.6 Hz, 2H), 2.92 – 2.86 (m, 2H), 1.78 – 1.70 (m, 2H), 1.61 – 1.55 (m, 2H), 1.34 (p, J = 7.0 Hz, 2H), 1.29 – 1.22 (m, 4H), 1.19 – 1.12 (m, 8H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 205.2, 150.9, 134.4, 132.1, 118.8, 114.0, 112.7, 42.2, 39.8, 27.6, 27.3, 27.3, 27.3, 27.0, 26.7, 26.5, 25.6, 25.4; HRMS (ESI-TOF) m/z calc for $C_{18}H_{28}NO$ [M+H^{+}] 274.2171. Found 274.2175; IR (film, CH_2Cl_2) *v*: 3307, 2928, 2855, 1633, 1573, 1517, 1459, 1326, 1246, 1162, 746 cm^{-1}.



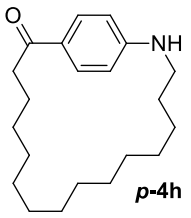
***p*-4g**

2-aza-1(1,4)-Benzenacyclotetradecaphan-14-one; 60% (13 mg; starting from 22 mg of **3g**); reaction in bath performed in degassed methanol (4 mL) for 4 h; slightly yellow solid; m.p. 102-103 °C; R*f* 0.34 (1:4 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.74 (d, J = 8.7 Hz, 2H), 6.67 (d, J = 8.7 Hz, 2H), 4.39 (bs, 1H), 3.42 – 3.36 (m, 2H), 2.85 – 2.79 (m, 2H), 1.71 – 1.65 (m, 2H), 1.59 (dt, J = 12.1, 6.7 Hz, 2H), 1.22 – 1.12 (m, 4H), 1.12 – 1.04 (m, 4H), 1.03 – 0.92 (m, 4H), 0.73 – 0.65 (m, 2H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 202.3, 152.7, 130.8, 128.1, 113.6, 43.2, 38.1, 29.0, 28.7, 2x28.1, 28.1, 27.2, 26.9, 26.8, 24.9; HRMS (ESI-TOF) m/z calc for $C_{18}H_{28}NO$ [M+H^{+}] 274.2171. Found 274.2175; IR (film, CH_2Cl_2) *v*: 3351, 2926, 2855, 1650, 1596, 1532, 1328, 1217, 1177, 831 cm^{-1}.



***o*-4h**

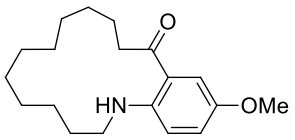
2,3,4,5,6,7,8,9,10,11,12,13,14,15-tetradecahydrobenzo[*b*][1]azacyclooctadecin-16(1*H*)-one; 45% (21 mg; starting from 47 mg of **3h**); reaction in bath performed in degassed methanol (7 mL) for 6 h; yellow solid; m.p. 71-72 °C; R*f* 0.52 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.07 (bs, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 6.71 (d, J = 8.5 Hz, 1H), 6.56 (t, J = 7.5 Hz, 1H), 3.26 (q, J = 5.3 Hz, 2H), 2.99 – 2.95 (m, 2H), 1.77 – 1.64 (m, 4H), 1.53 – 1.45 (m, 2H), 1.41 – 1.23 (m, 18H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 203.0, 151.5, 134.7, 131.9, 117.8, 113.6, 111.9, 41.9, 38.3, 28.6, 28.4, 2x28.3, 28.1, 27.70, 27.65, 27.3, 27.2, 26.5, 25.7, 24.0; HRMS (ESI-TOF) m/z calc for $C_{21}H_{34}NO$ [M+H^{+}] 316.2640. Found 316.2645; IR (film, CH_2Cl_2) *v*: 3219, 2924, 2855, 1638, 1574, 1519, 1458, 1332, 1213, 743, 613 cm^{-1}.



***p*-4h**

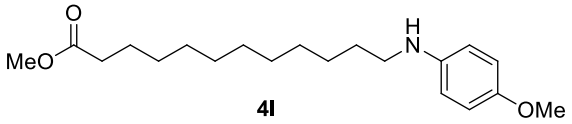
2-Aza-1(1,4)-benzenacycloheptadecaphan-17-one; 45% (13 mg; starting from 47 mg of **3h**); reaction in bath performed in degassed methanol (7 mL) for 6 h; white solid; m.p.; 80-81 °C; R*f* 0.13 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.82 (d, J = 8.7 Hz, 2H), 6.57 (d, J = 8.7 Hz, 2H), 4.28 (bs, 1H), 3.31 (q, J = 6.2 Hz, 2H), 2.80 (t, J = 6.9 Hz, 2H), 1.76 (p, J = 6.6 Hz, 2H), 1.63 – 1.53 (m, 2H), 1.35 – 1.07 (m, 20H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 200.5, 152.4, 131.1, 126.4, 111.6, 42.2, 37.0, 29.2, 29.1, 28.5, 28.4, 28.3, 28.2, 28.1, 27.9, 27.8, 27.6, 26.3, 24.9; HRMS (ESI-TOF) m/z calc for $C_{21}H_{34}NO$ [M+H^{+}] 316.2640. Found

316.2644; IR (film, CH_2Cl_2) *v*: 3354, 2925, 2853, 1649, 1595, 1536, 1460, 1338, 1270, 1178, 827 cm^{-1}.



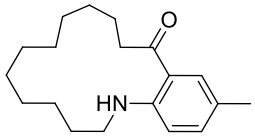
***o*-4l**

15-Methoxy-1,2,3,4,5,6,7,8,9,10,11,12-dodecahydro-13*H*-benzo[*b*][1]azacyclopentadecin-13-one; 75% (6 mg; starting from 8 mg of **3l**); reaction in bath performed in degassed cyclohexane (1.5 mL) for 3 h; yellow oil; R*f* 0.73 (1:2 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 8.27 (bs, 1H), 7.19 (d, *J* = 3.0 Hz, 1H), 7.03 (dd, *J* = 9.2, 3.0 Hz, 1H), 6.74 (d, *J* = 9.2 Hz, 1H), 3.78 (s, 3H), 3.32 – 3.26 (m, 2H), 2.90 – 2.85 (m, 2H), 1.77 – 1.70 (m, 2H), 1.58 – 1.51 (m, 2H), 1.34 – 1.12 (m, 14H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 204.5, 148.8, 146.1, 122.8, 118.8, 115.5, 114.3, 56.3, 42.7, 39.9, 27.7, 27.3, 27.2, 27.0, 26.6, 26.3, 25.5, 25.3; HRMS (ESI-TOF) m/z calc for $C_{19}H_{30}NO_2$ [M+H$^+$] 304.2277. Found 304.2275; IR (film, CH_2Cl_2) *v*: 3322, 2927, 2855, 1641, 1517, 1461, 1275, 1218, 1176, 1047, 812 cm^{-1}.



4l

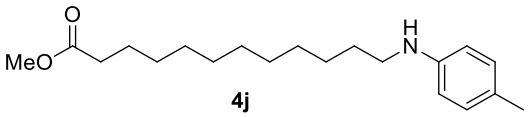
Methyl 12-((4-methoxyphenyl)amino)dodecanoate; 20% (7 mg; starting from 31 mg of **3l**); reaction in bath performed in degassed methanol (4 mL) for 5 h; waxy solid; R*f* 0.50 (1:2 AcOEt in hexanes); ^{1}H NMR (600 MHz, chloroform-*d*) δ 6.80 – 6.77 (m, 2H), 6.64 – 6.60 (m, 2H), 3.75 (s, 3H), 3.66 (s, 3H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.30 (t, *J* = 7.6 Hz, 2H), 1.65 – 1.57 (m, 4H), 1.40 – 1.24 (m, 14H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 174.5, 152.5, 142.3, 115.1, 114.7, 56.0, 51.6, 45.6, 34.3, 29.68, 2x29.64, 29.57, 29.55, 29.4, 29.3, 27.3, 25.1; HRMS (ESI-TOF) m/z calc for $C_{20}H_{34}NO_3$ [M+H$^+$] 336.2539. Found 336.2546; IR (film, CH_2Cl_2) *v*: 3392, 2919, 2847, 1729, 1522, 1466, 1251, 1237, 1178, 1033, 825 cm^{-1}.



***o*-4j**

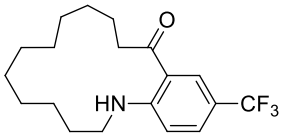
15-Methyl-1,2,3,4,5,6,7,8,9,10,11,12-dodecahydro-13*H*-benzo[*b*][1]azacyclopentadecin-13-one; 92% (12 mg; starting from 13 mg of **3j**); reaction in bath performed in degassed cyclohexane (3 mL) for 3 h; yellow waxy solid; R*f* 0.43 (1:9 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 8.46 (bs, 1H), 7.46 (d, J = 2.1 Hz, 1H), 7.16 (dd, J = 8.6, 2.1 Hz, 1H), 6.69 (d, J = 8.6 Hz, 1H), 3.29 (q, J = 5.5 Hz, 2H), 2.90 – 2.86 (m, 2H), 2.26 (s, 3H), 1.76 – 1.70 (m, 2H), 1.59 – 1.52 (m, 2H), 1.38 – 1.27 (m, 2H), 1.27 – 1.21 (m, 4H), 1.19 – 1.13 (m, 8H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 205.0, 149.0, 135.6, 131.8, 122.8, 118.8, 112.9, 42.4, 39.7, 27.7, 27.3, 27.3, 27.2, 27.0, 26.6, 26.4, 25.5, 25.4, 20.5; HRMS (ESI-TOF) m/z calc for

$C_{19}H_{30}NO$ [M+H$^+$] 288.2327. Found 288.2329; IR (film, CH_2Cl_2) *v*: 3314, 2927, 2855, 1735, 1637, 1573, 1522, 1460, 1424, 1321, 1261, 1175, 1103, 972, 809 cm^{-1}.



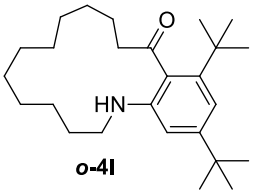
4j

Methyl 12-(*p*-tolylamino)dodecanoate; 18% (7 mg; starting from 35 mg of **3j**); reaction in bath performed in degassed methanol (5 mL) for 4 h; yellow solid; m.p. 68-69 °C; R*f* 0.25 (1:9 AcOEt in hexanes); ^{1}H NMR (600 MHz, chloroform-*d*) δ 6.99 (d, J = 8.0 Hz, 2H), 6.58 (d, *J* = 8.0 Hz, 2H), 3.67 (s, 3H), 3.08 (t, *J* = 7.2 Hz, 2H), 2.30 (t, *J* = 7.6 Hz, 2H), 2.24 (s, 3H), 1.64 – 1.59 (m, 4H), 1.33 – 1.25 (m, 14H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 174.5, 145.8, 130.2, 129.9, 113.6, 51.6, 45.0, 34.3, 29.7, 29.64, 2x29.56, 29.4, 29.3, 27.3, 25.1, 20.5; HRMS (ESI-TOF) m/z calc for $C_{20}H_{34}NO_2$ [M+H$^+$] 288.2327. Found 288.2329; IR (film, CH_2Cl_2) *v*: 3399, 2916, 2850, 1731, 1619, 1525, 1469, 1436, 1322, 1269, 1230, 1203, 1171, 815, 802, 717, 508 cm^{-1}.



***o*-4k**

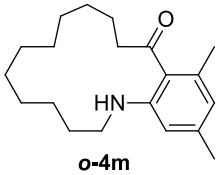
15-(Trifluoromethyl)-1,2,3,4,5,6,7,8,9,10,11,12-dodecahydro-13*H*-benzo[*b*][1]azacyclopentadecin-13-one; 86% (19 mg; starting from 22 mg of **3k**); reaction in bath performed in degassed cyclohexane (3 mL) for 4 h; yellow oil; R*f* 0.62 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.97 (bs, 1H), 7.91 (d, *J* = 2.2 Hz, 1H), 7.51 (dd, *J* = 9.0, 2.2 Hz, 1H), 6.79 (d, *J* = 9.0 Hz, 1H), 3.38 – 3.29 (m, 2H), 2.94 – 2.89 (m, 2H), 1.79 – 1.71 (m, 2H), 1.64 – 1.57 (m, 2H), 1.35 (p, *J* = 6.8 Hz, 2H), 1.28 – 1.23 (m, 4H), 1.18 – 1.13 (m, 8H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 204.8, 152.6, 130.8 (q, *J* = 3.1 Hz), 129.5 (q, *J* = 4.1 Hz), 124.8 (q, *J* = 270.3 Hz), 117.5, 115.7 (d, *J* = 33.1 Hz), 112.6, 42.3, 39.7, 27.5, 27.4, 2x27.3, 27.0, 26.7, 26.6, 25.6, 25.2; HRMS (ESI-TOF) m/z calc for $C_{19}H_{27}NOF_3$ [M+H$^+$] 342.2045. Found 342.2047; IR (film, CH_2Cl_2) *v*: 3302, 2929, 2856, 1643, 1577, 1536, 1322, 1112, 1083, 818, 610 cm^{-1}.



***o*-4l**

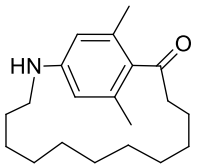
14,16-*di-tert*-Butyl-1,2,3,4,5,6,7,8,9,10,11,12-dodecahydro-13*H*-benzo[*b*][1]azacyclopentadecin-13-one; 85% (23 mg; starting from 27 mg of **3l**); reaction in bath performed in degassed cyclohexane (4 mL) for 3 h; waxy solid; R*f* 0.38 (1:9 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 6.92 (d, *J* = 1.6 Hz, 1H), 6.60 (d, *J* = 1.6 Hz, 1H), 3.11 – 2.96 (m, 4H), 1.85 – 1.69 (m, 4H), 1.42 – 1.27 (m, 32H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 214.8, 151.7, 145.5, 143.9, 127.3, 114.3, 106.9, 45.1, 43.6, 36.6, 35.1, 32.5,

31.5, 29.5, 26.6, 26.4, 26.3, 25.8, 25.5, 25.3, 23.3, 21.0; HRMS (ESI-TOF) m/z calc for $C_{26}H_{44}NO$ [M+H$^+$] 386.3423. Found 386.3424; IR (film, CH_2Cl_2) *v*: 3387, 2927, 2856, 1687, 1600, 1561, 1460, 1362, 1313, 1244, 979, 847 cm^{-1}.



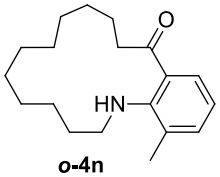
***o*-4m**

14,16-Dimethyl-1,2,3,4,5,6,7,8,9,10,11,12-dodecahydro-13*H*-benzo[*b*][1]azacyclopentadecin-13-one; 58% (19 mg; starting from 33 mg of **3m**); reaction in bath performed in degassed cyclohexane (6 mL) for 6 h; yellow solid; m.p.77-78 °C; R*f* 0.52 (1:9 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 6.34 (s, 1H), 6.33 (s, 1H), 5.03 (bs, 1H), 3.13 – 3.09 (m, 2H), 2.77 (t, *J* = 6.9 Hz, 2H), 2.27 (s, 3H), 2.26 (s, 3H), 1.73 – 1.66 (m, 2H), 1.59 – 1.56 (m, 2H), 1.40 – 1.25 (m, 16H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 210.9, 146.2, 141.0, 135.3, 124.7, 120.0, 109.8, 44.3, 42.5, 28.7, 27.2, 26.8, 26.4, 26.3, 25.4, 25.2, 25.0, 24.1, 21.9, 21.2; HRMS (ESI-TOF) m/z calc for $C_{20}H_{32}NO$ [M+H$^+$] 302.2484. Found 302.2486; IR (film, CH_2Cl_2) *v*: 3390, 2926, 2855, 1686, 1645, 1605, 1573, 1456, 1326, 1219, 822 cm^{-1}.



***p*-4m**

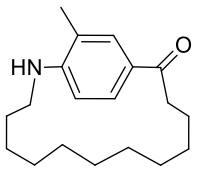
1^3,1^5-Dimethyl-2-aza-1(1,4)-benzenacyclotetradecaphan-14-one; 24% (8 mg; starting from 33 mg of **3m**); reaction in bath performed in degassed cyclohexane (6 mL) for 6 h; yellow oil; R*f* 0.17 (1:9 AcOEt in hexanes); ^{1}H NMR (500 MHz, chloroform-*d*) δ 6.29 (s, 2H), 3.64 (bs, 1H), 3.31 – 3.28 (m, 2H), 2.69 – 2.66 (m, 2H), 2.21 (s, 6H), 1.58 – 1.53 (m, 2H), 1.50 – 1.47 (m, 2H), 1.27 – 1.24 (m, 4H), 1.10 – 0.96 (m, 8H), 0.86 – 0.82 (m, 2H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 211.8, 149.0, 135.4, 130.7, 113.4, 44.6, 42.9, 28.6, 28.34, 28.28, 27.92, 27.88, 27.7, 27.1, 25.4, 24.7, 20.7; HRMS (ESI-TOF) m/z calc for $C_{20}H_{32}NO$ [M+H$^+$] 302.2484. Found 302.2486; IR (film, CH_2Cl_2) *v*: 3377, 2925, 2853, 1670, 1604, 1512, 1457, 1332, 1260, 1174, 840 cm^{-1}.



***o*-4n**

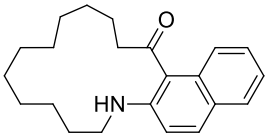
17-Methyl-1,2,3,4,5,6,7,8,9,10,11,12-dodecahydro-13*H*-benzo[*b*][1]azacyclopentadecin-13-one; 15% (5 mg; starting from 32 mg of **3n**); reaction in bath performed in degassed cyclohexane (6 mL) for 7 h; yellow waxy solid; R*f* 0.78 (15:85 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.89 (bs, 1H), 7.59 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.20 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.74 (t, *J* = 7.6 Hz, 1H), 3.19 (t, *J* = 6.1 Hz, 2H), 2.98 – 2.95 (m, 2H), 2.33 (s, 3H), 1.80 – 1.75 (m, 2H), 1.45 – 1.40 (m, 2H), 1.31 – 1.20 (m, 14H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 205.2, 151.8, 136.7, 129.4, 129.1, 125.3, 118.0, 48.0, 39.7, 30.5, 27.1, 27.0, 26.4, 26.1, 26.0,

25.5, 25.1, 24.5, 21.0; HRMS (ESI-TOF) m/z calc for $C_{19}H_{30}NO$ [M+H$^+$] 288.2327. Found 288.2326; IR (film, CH_2Cl_2) *v*: 3322, 2925, 2854, 1643, 1595, 1502, 1456, 1226, 749 cm^{-1}.



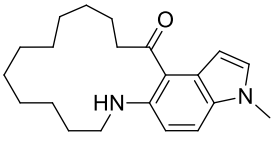
***p*-4n**

1^2-Methyl-2-aza-1(1,4)-benzenacyclotetradecaphan-14-one; 41% (13 mg; starting from 32 mg of **3n**); reaction in bath performed in degassed cyclohexane (6 mL) for 7 h; yellow waxy solid; R*f* 0.21 (15:85 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.68 – 7.64 (m, 2H), 6.72 – 6.69 (m, 1H), 4.02 (bs, 1H), 3.50 – 3.44 (m, 2H), 2.85 – 2.79 (m, 2H), 2.17 (s, 3H), 1.72 – 1.64 (m, 2H), 1.61 – 1.59 (m, 2H), 1.15 – 1.11 (m, 4H), 1.10 – 1.05 (m, 4H), 1.00 – 0.92 (m, 4H), 0.70 – 0.62; ^{13}C NMR (101 MHz, chloroform-*d*) δ 202.6, 150.8, 130.8, 129.3, 127.2, 121.7, 110.6, 43.0, 38.1, 29.0, 28.8, 28.10, 28.07, 28.04, 27.2, 26.93, 26.89, 24.6, 17.5.; HRMS (ESI-TOF) m/z calc for $C_{19}H_{30}NO$ [M+H$^+$] 288.2327. Found 288.2331; IR (film, CH_2Cl_2) *v*: 3392, 2926, 2854, 1654, 1595, 1527, 1458, 1289, 1145, 814, 739, 528 cm^{-1}.



***o*-4o**

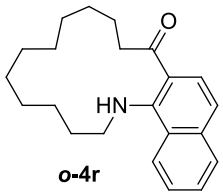
7,8,9,10,11,12,13,14,15,16,17,18-Dodecahydro-19*H*-naphtho[2,1-*b*][1]azacyclopentadecin-19-one; bath: 50% (16 mg; starting from 32 mg of **3o**); reaction was performed in degassed cyclohexane (5 mL) for 4 h; flow: 61% (18 mg; starting from 30 mg of **3o**); reaction was performed in degassed cyclohexane (10 mL) for 20 min; yellow oil; R*f* 0.73 (1:9 AcOEt in hexanes); ^{1}H NMR (500 MHz, benzene-d_6) δ 7.67 (bs, 1H), 7.63 – 7.59 (m, 2H), 7.56 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.30 (t, *J* = 8.3 Hz, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 9.2 Hz, 1H), 3.28 (q, *J* = 5.5 Hz, 2H), 2.96 (t, *J* = 6.3 Hz, 2H), 1.63 – 1.57 (m, 2H), 1.53 – 1.48 (m, 2H), 1.30 (p, *J* = 7.0 Hz, 2H), 1.23 – 1.10 (m, 10H), 1.02 – 0.96 (m, 2H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 207.5, 146.9, 133.8, 133.2, 128.7, 127.3, 126.5, 124.6, 122.1, 115.7, 114.6, 44.2, 42.1, 29.2, 27.3, 27.0, 26.6, 26.4, 26.2, 25.9, 25.2, 25.1; HRMS (ESI-TOF) m/z calc for $C_{22}H_{30}NO$ [M+H$^+$] 324.2327. Found 324.2332; IR (film, CH_2Cl_2) *v*: 3348, 2926, 2855, 1626, 1563, 1511, 1431, 1343, 1188, 1155, 811, 746 cm^{-1}.



***o*-4p**

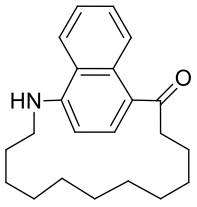
3-Methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-[1]azacyclopentadecino[3,2-*e*]indol-18(3*H*)-one; bath: 25% (12 mg; starting from 48 mg of **3p**); reaction was performed in degassed cyclohexane (8 mL) for 5 h; flow: 57% (12 mg; starting from 21 mg of **3p**);

reaction was performed in degassed cyclohexane (8 mL) for 30 min; yellow oil; R*f* 0.33 (1:9 AcOEt in hexanes); ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.79 (bs, 1H), 7.35 (d, *J* = 9.0 Hz, 1H), 7.03 (d, *J* = 3.2 Hz, 1H), 6.81 – 6.73 (m, 1H), 6.50 (d, *J* = 3.1 Hz, 1H), 3.77 (s, 3H), 3.36 – 3.32 (m, 2H), 3.12 – 3.09 (m, 2H), 1.85 – 1.80 (m, 2H), 1.63 – 1.58 (m, 2H), 1.36 (p, *J* = 7.1 Hz, 2H), 1.29 – 1.17 (m, 12H); ^{13}C NMR (126 MHz, chloroform-*d*) δ 204.3, 129.2, 127.6, 116.5, 109.1, 101.9, 43.4, 42.9, 33.1, 28.5, 27.8, 27.2, 26.8, 26.7, 26.0, 25.6, 24.5; HRMS (ESI-TOF) m/z calc for $C_{21}H_{31}N_2O$ [M+H$^+$] 327.2436. Found 327.2431; IR (film, CH_2Cl_2) *v*: 3298, 2925, 2854, 1619, 1598, 1510, 1426, 1361, 1332, 1294, 1174, 1092, 793, 719 cm^{-1}.



***o*-4r**

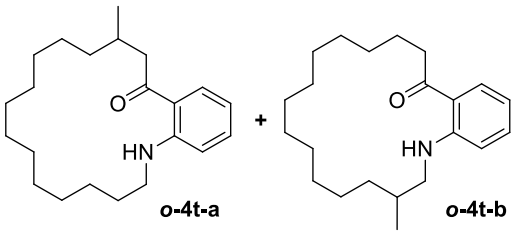
1,2,3,4,5,6,7,8,9,10,11,12-Dodecahydro-13*H*-naphtho[1,2-*b*][1]azacyclopentadecin-13-one; bath: 28% (9 mg; starting from 32 mg of **3r**); reaction was performed in degassed cyclohexane (5 mL) for 5 h; flow: 39% (13 mg; starting from 33 mg of **3r**); reaction was performed in degassed cyclohexane (10 mL) for 25 min; yellow oil; R*f* 0.67 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.35 (bs, 1H), 8.26 (d, *J* = 8.5 Hz, 1H), 7.73 – 7.69 (m, 2H), 7.50 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.38 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 1H), 3.66 (t, *J* = 5.9 Hz, 2H), 3.03 – 2.99 (m, 2H), 1.88 – 1.81 (m, 2H), 1.32 – 1.19 (m, 16H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 203.8, 153.9, 137.6, 128.6, 128.1, 127.9, 2x126.8, 124.2, 118.2, 117.4, 51.6, 39.4, 31.7, 27.2, 27.1, 26.6, 26.3, 25.9, 25.5, 25.4, 24.5.; HRMS (ESI-TOF) m/z calc for $C_{22}H_{30}NO$ [M+H$^+$] 324.2327. Found 324.2331; IR (film, CH_2Cl_2) *v*: 3290, 2926, 2854, 1618, 1569, 1510, 1445, 1346, 1228, 1146, 1065, 795 cm^{-1}.



***p*-4r**

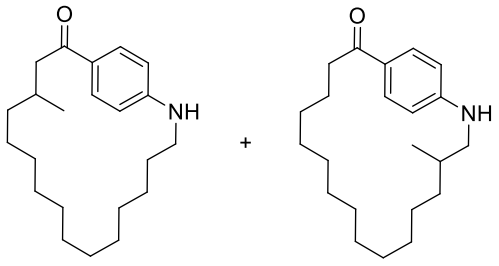
2-Aza-1(1,4)-naphthalenacyclotetradecaphan-14-one; bath: 34% (11 mg; starting from 32 mg of **3r**); reaction was performed in degassed cyclohexane (5 mL) for 5 h; flow: 44% (15 mg; starting from 33 mg of **3r**); reaction was performed in degassed cyclohexane (10 mL) for 25 min; yellow solid; m.p. 164-165 °C; R*f* 0.16 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.94 (dd, *J* = 8.7, 1.3 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.57 (ddd, *J* = 8.4, 6.7, 1.3 Hz, 1H), 7.46 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 6.69 (d, *J* = 8.3 Hz, 1H), 5.01 (s, 1H), 3.61 (t, *J* = 5.9 Hz, 2H), 3.01 – 2.94 (m, 2H), 1.77 – 1.63 (m, 4H), 1.27 – 1.14 (m, 4H), 1.08 – 1.02 (m, 4H), 0.98 – 0.93 (m, 2H), 0.90 – 0.85 (m, 2H), 0.70 – 0.64 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.4, 147.7, 132.31, 132.29, 128.0, 127.0, 125.2, 123.8, 122.9, 119.6, 103.4, 42.8, 41.2, 28.8, 28.6, 27.93, 27.89, 27.6, 27.3, 27.04, 27.02, 25.0; HRMS

(ESI-TOF) m/z calc for $C_{22}H_{30}NO$ [M+H$^+$] 324.2327. Found 324.2330; IR (film, CH_2Cl_2) *v*: 3056, 2920, 2851, 1648, 1442, 1399,1280, 808, 779, 741 cm^{-1}.



***o*-4t-a** ***o*-4t-b**

14-Methyl-2,3,4,5,6,7,8,9,10,11,12,13,14,15-tetradecahydrobenzo[*b*][1]azacyclooctadecin-16(1*H*)-one and **3-Methyl-2,3,4,5,6,7,8,9,10,11,12,13,14,15-tetradecahydrobenzo[*b*][1]azacyclooctadecin-16(1*H*)-one**; inseparable mixture of isomers ***o*-4t-a** and ***o*-3t-b** in ratio 1.0:1.0; bath: 43% (22 mg; starting from 51 mg of mixture of **3t-a** and **3t-b** in ratio 1.0:1.1); reaction was performed in degassed cyclohexane (5 mL) for 6 h; flow: 54% (14 mg; starting from 26 mg of mixture of **3t-a** and **3t-b** in ratio 1.0:1.1); reaction was performed in degassed cyclohexane (12 mL) for 35 min; waxy yellow solid; R*f* 0.73 (1:9 AcOEt in hexanes); ***o*-4t-a** selected signals: ^{1}H NMR (600 MHz, chloroform-*d*) δ 9.10 (bs, 1H), 2.86 (dd, *J* = 15.9, 3.2 Hz, 1H), 2.79 (dd, *J* = 15.8, 10.4 Hz, 1H), 2.24 – 2.17 (m, 1H), 1.00 (d, *J* = 2.4 Hz, 3H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 202.5, 46.8, 41.8, 34.0, 28.65, 20.2; ***o*-4t-b** selected signals: ^{1}H NMR (600 MHz, chloroform-*d*) δ 9.16 (s, 1H), 3.00 (ddd, *J* = 16.1, 8.2, 3.7 Hz, 1H), 2.93 (ddd, *J* = 15.8, 7.7, 3.5 Hz, 1H), 2.90 – 2.86 (m, 1H), 1.88 – 1.80 (m, 1H), 0.99 (d, *J* = 2.4 Hz, 3H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 202.8, 151.4, 48.5, 38.0, 32.6, 23.9, 18.2, ; HRMS (ESI-TOF) m/z calc for $C_{22}H_{36}NO$ [M+H$^+$] 330.2797. Found 330.2806; IR (film, CH_2Cl_2) *v*: 3294, 2925, 2854, 1638, 1606, 1575, 1520, 1459, 1208, 1161, 744 cm^{-1}.

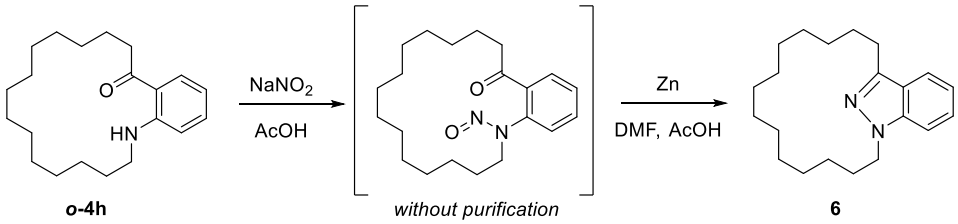


***p*-4t-a** ***p*-4t-b**

15-Methyl-2-aza-1(1,4)-benzenacycloheptadecaphan-17-one and **4-Methyl-2-aza-1(1,4)-benzenacycloheptadecaphan-17-one**; inseparable mixture of isomers ***p*-4t-a** and ***p*-3t-b** in ratio 1.0:1.2; bath: 29% (15 mg; starting from 51 mg of mixture of **3t-a** and **3t-b** in ratio 1.0:1.1); reaction was performed in degassed cyclohexane (5 mL) for 6 h; flow: 35% (9mg; starting from 26 mg of mixture of **3t-a** and **3t-b** in ratio 1.0:1.1); reaction was performed in degassed cyclohexane (12 mL) for 35 min; waxy yellow solid; R*f* 0.73 (1:9 AcOEt in hexanes); ***p*-4t-a** selected signals: ^{1}H NMR (600 MHz, chloroform-*d*) δ 4.29 (bs, 1H), 3.36 – 3.29 (m, 1H), 3.29 – 3.23 (m, 1H), 2.97 (dd, *J* = 12.7, 8.3 Hz, 1H), 2.36 (dd, *J* = 12.7, 5.8 Hz, 1H), 2.12 – 2.05 (m, 1H), 0.99 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 45.3, 42.0, 31.3, 21.1; ***p*-**

4t-b selected signals: ^{1}H NMR (600 MHz, chloroform-*d*) δ 4.45 (bs, 1H), 3.16 – 3.06 (m, 2H), 2.94 – 2.88 (m, 1H), 2.69 – 2.61 (m, 1H), 1.86 – 1.79 (m, 1H), 0.91 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (151 MHz, chloroform-*d*) δ 48.7, 36.8, 31.0, 18.2; HRMS (ESI-TOF) m/z calc for $C_{22}H_{36}NO$ [M+H^{+}] 330.2797. Found 330.2804; IR (film, CH_2Cl_2) *v*: 3357, 2925, 2853, 1648, 1596, 1535, 1460, 1339, 1281, 1178, 827 cm^{-1}.

8. Synthesis of indazole 6 *via N*-nitrosation of o-4h, and subsequent reductive heterocyclization.



***o*-4h** *without purification* **6**

N-nitrosation reaction and subsequent reductive heterocyclization was performed according to the literature procedure with small modification. To a solution of *ortho*-cyclophane ***o*-4h** (17 mg, 0.054 mmol) in acetic acid (0.5 mL) $NaNO_2$ was added (7.5 mg, 0.108 mmol;,2.0 equiv). The reaction was stirred at room temperature overnight. After complete conversion of substrate ***o*-4h** (TLC monitoring, 1:9 AcOEt:hexanes) H_2O (0.5 mL) was added. The reaction mixture was washed with CH_2Cl_2 (3x 1.0 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to give the crude nitrosoaniline as a yellow oil, which was used to the next step without farther purification.

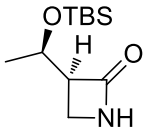
To a solution of crude nitrosoaniline (0.054 mmol) in mixture of DMF (0.5 mL) and acetic acid (0.5 mL) zinc dust (18 mg, 0.27 mmol, 5.0 equiv.) was added at 0 °C. The reaction mixture was stirred at room temperature for one hour, then heated at 100 °C overnight. After complete conversion of nitrosoaniline (TLC monitoring, 1:9 AcOEt:hexanes) H_2O (0.5 mL) was added. The reaction mixture was washed with CH_2Cl_2 (3x 1.0 mL). The combined organic layers were dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to give the crude product which was preabsorbed onto silica gel, and then purified by flash chromatography to afford 14 mg (83%, after two steps) of indazole **6** as a slightly yellow oil. R*f* 0.48 (1:9 AcOEt in hexanes); ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.71 – 7.65 (m, 1H), 7.37 – 7.31 (m, 2H), 7.09 (ddd, *J* = 7.9, 4.7, 2.9 Hz, 1H), 4.39 – 4.35 (m, 2H), 3.04 – 2.99 (m, 2H), 1.91 – 1.78 (m, 4H), 1.32 – 1.10 (m, 20H); ^{13}C NMR (101 MHz, chloroform-*d*) δ 145.1, 140.5, 125.9, 123.1, 120.7, 119.4, 109.1, 48.7, 30.0, 28.9, 28.22, 28.17, 27.98, 2x27.86,

27.22, 27.17, 26.8, 2x26.4, 26.0; HRMS (ESI-TOF) m/z calc for $C_{21}H_{33}N_2$ [M+H$^+$] 313.2644. Found 313.2647; IR (film, CH_2Cl_2) *v*: 2925, 2854, 1614, 1503, 1458, 1367, 1309, 1177, 1134, 1007, 741 cm^{-1}.

9. Literature:

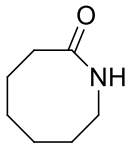
1. P. Szcześniak and B. Furman, *Chemical Communications*, 2022, **58**, 1898-1901.
2. C. Crauste, M. Froeyen, J. Anné and P. Herdewijn, *European Journal of Organic Chemistry*, 2011, **2011**, 3437-3449.
3. D. Dev, T. Kalita, T. Mondal and B. Mandal, *Advanced Synthesis & Catalysis*, 2021, **363**, 1427-1435.
4. V. P. Srivastava, R. Patel, Garima and L. D. S. Yadav, *Chemical Communications*, 2010, **46**, 5808-5810.
5. K. Hyodo, G. Hasegawa, N. Oishi, K. Kuroda and K. Uchida, *The Journal of Organic Chemistry*, 2018, **83**, 13080-13087.
6. R. S. Phatake, N. B. Nechmad, O. Reany and N. G. Lemcoff, *Advanced Synthesis & Catalysis*, 2022, **364**, 1465-1472.
7. P. Petiot and A. Gagnon, *European Journal of Organic Chemistry*, 2013, **2013**, 5282-5289.
8. A.-M. Preda, M. Krasowska, L. Wrobel, P. Kitschke, P. C. Andrews, J. G. MacLellan, L. Mertens, M. Korb, T. Rüffer, H. Lang, A. A. Auer and M. Mehring, *Beilstein Journal of Organic Chemistry*, 2018, **14**, 2125-2145.
9. A. F. M. M. Rahman, T. Murafuji, M. Ishibashi, Y. Miyoshi and Y. Sugihara, *Journal of Organometallic Chemistry*, 2004, **689**, 3395-3401.
10. D. M. T. Chan, *Tetrahedron Letters*, 1996, **37**, 9013-9016.
11. Current Patent Assignee: HIBERCELL INC - WO2019/126730, 2019, A1 Location in patent: Paragraph 0305.
12. W. Deng, Y.-F. Wang, Y. Zou, L. Liu and Q.-X. Guo, *Tetrahedron Letters*, 2004, **45**, 2311-2315.
13. F. Mongin, R. Amara, B.-A. Ghenia, M. Hedidi, J. Khoury, H. Awad, E. Nassar, T. Roisnel, V. Dorcet, F. Chevallier, Z. Fajloun, J. Maillard, W. Erb, F. Lassagne, Y. Halauko, O. Ivashkevich, V. Matulis, M. Hamze, B. Baratte and S. Bach, 2017.
14. J. Yin and S. L. Buchwald, *J Am Chem Soc*, 2002, **124**, 6043-6048.
15. T. Ghosh, P. Maity and B. C. Ranu, *ChemistrySelect*, 2018, **3**, 4406-4412.
16. P. Maity, D. Kundu and B. C. Ranu, *Advanced Synthesis and Catalysis*, 2015, **357**, 3617-3626.
17. S. O'Sullivan, E. Doni, T. Tuttle and J. A. Murphy, *Angewandte Chemie International Edition*, 2014, **53**, 474-478.
18. J. Chen, J. Wang and T. Tu, *Chemistry – An Asian Journal*, 2018, **13**, 2559-2565.
19. C. A. Brown and V. K. Aggarwal, *Chemistry (Weinheim an der Bergstrasse, Germany)*, 2015, **21**, 13900-13903.
20. T. Tsunoda, A. Yamazaki, H. Iwamoto and S. Sakamoto, *Organic Process Research & Development*, 2003, **7**, 883-887.
21. D. Misiti, V. Rimatori and F. Gatta, *Journal of Heterocyclic Chemistry*, 1973, **10**, 689-696.

^{1}H NMR (400 MHz, Chloroform-*d*)



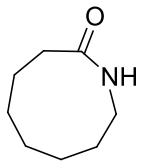
1a

^{1}H NMR (400 MHz, Chloroform-*d*)



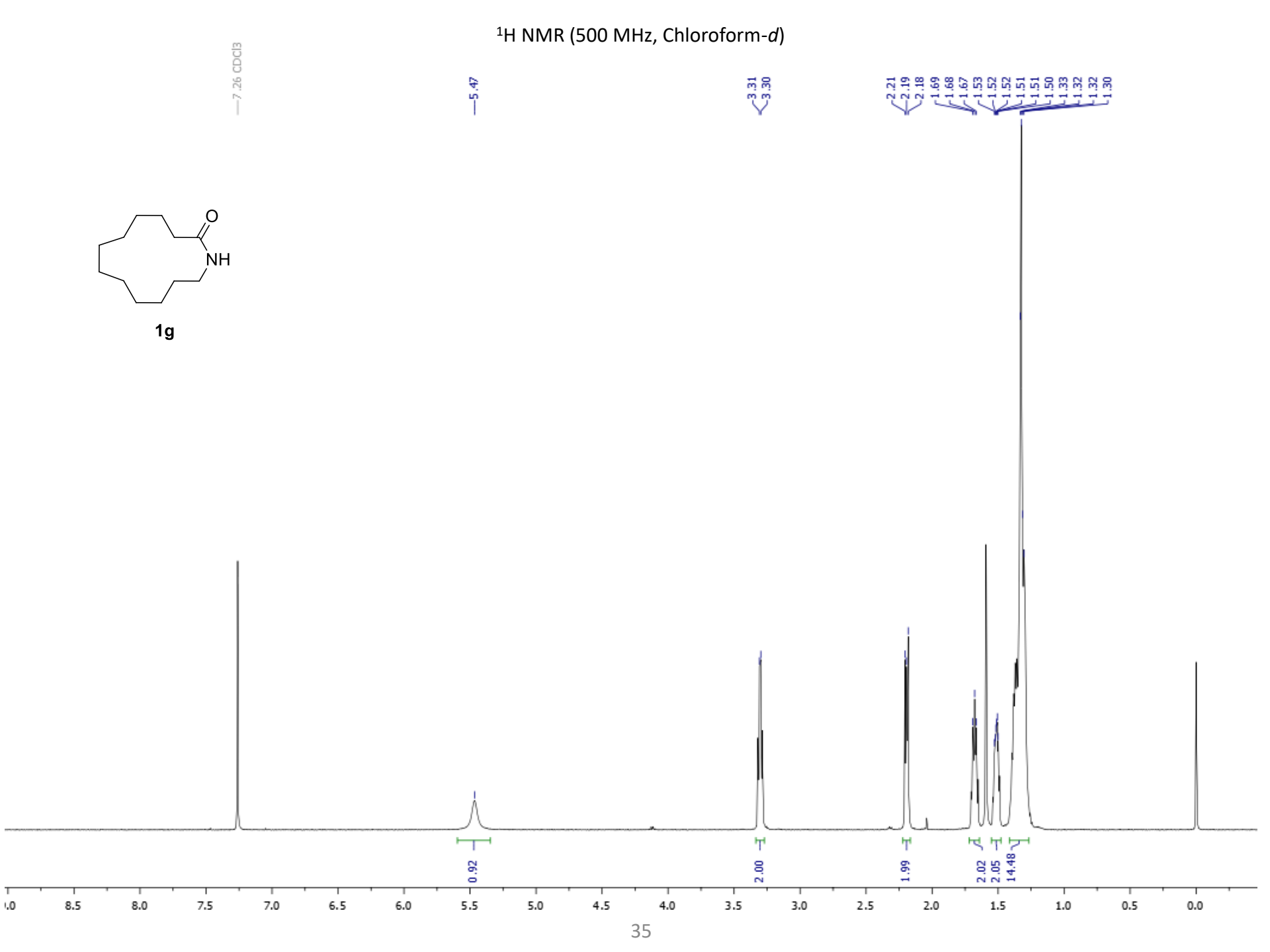
1e

^{1}H NMR (500 MHz, Chloroform-*d*)



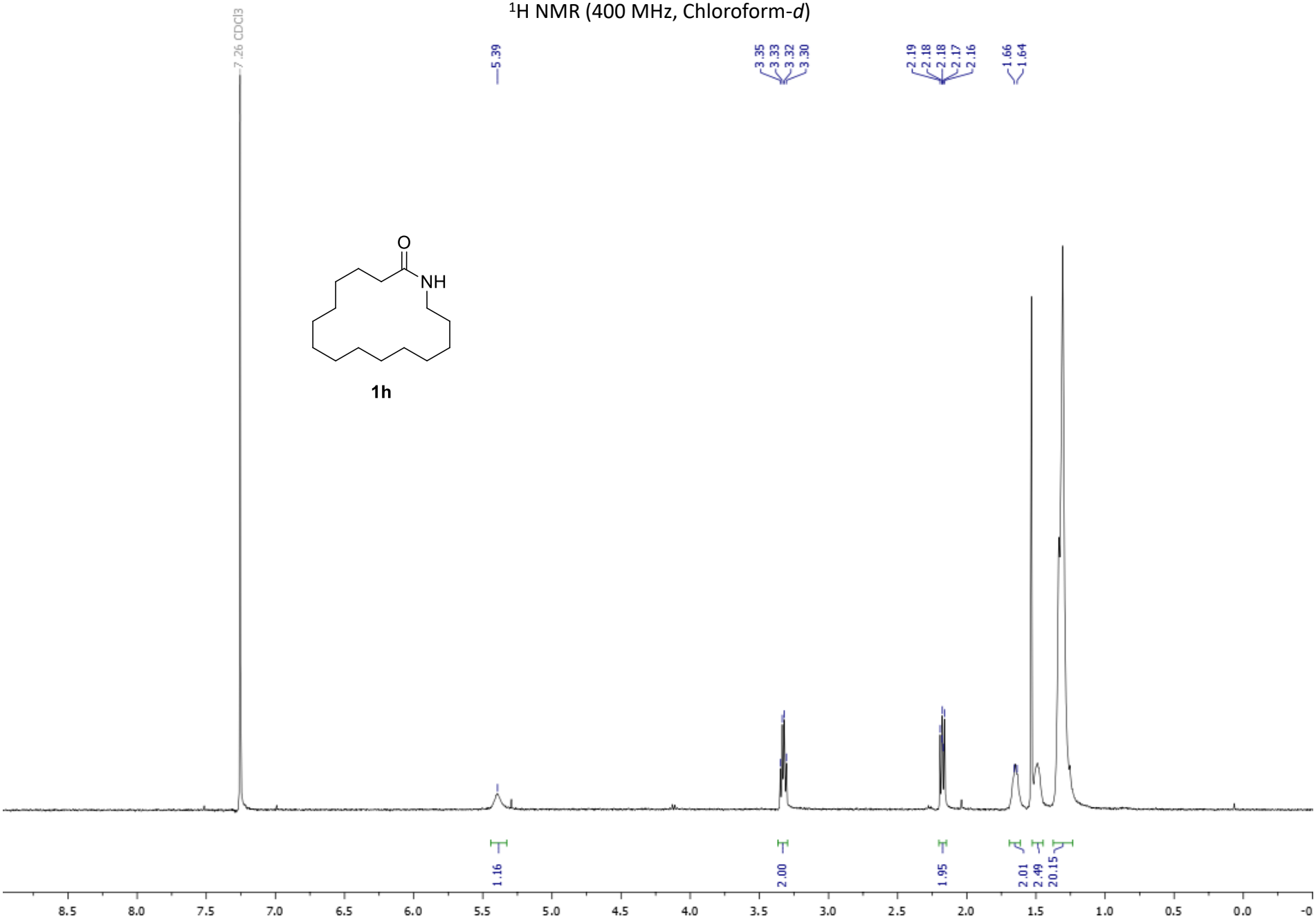
1f

^{1}H NMR (500 MHz, Chloroform-*d*)

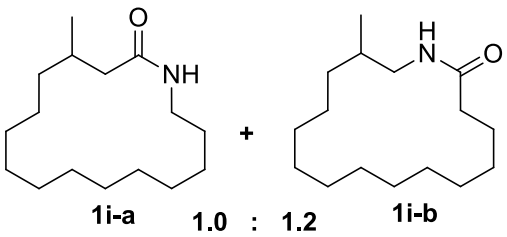


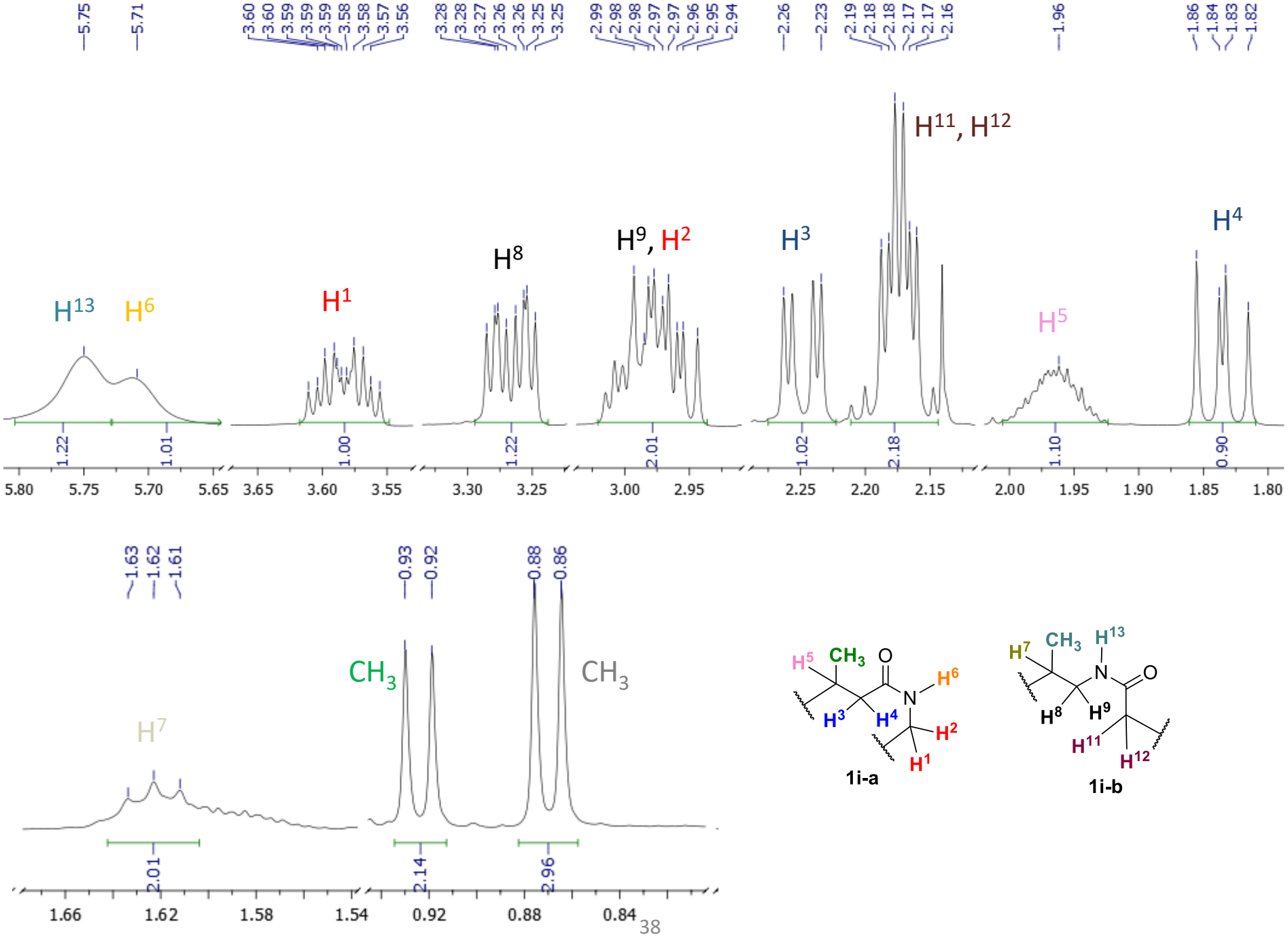
1g

^{1}H NMR (400 MHz, Chloroform-*d*)

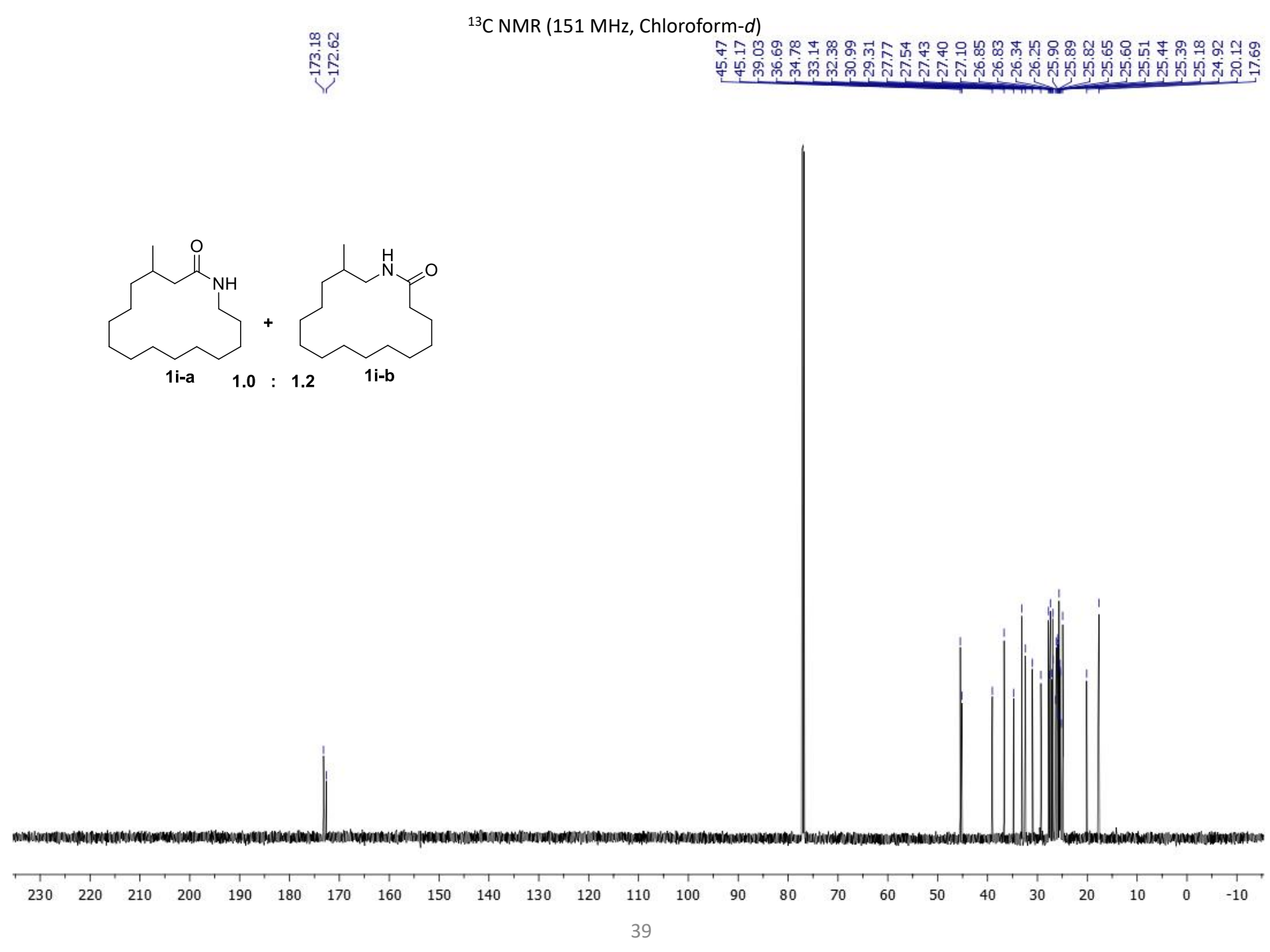


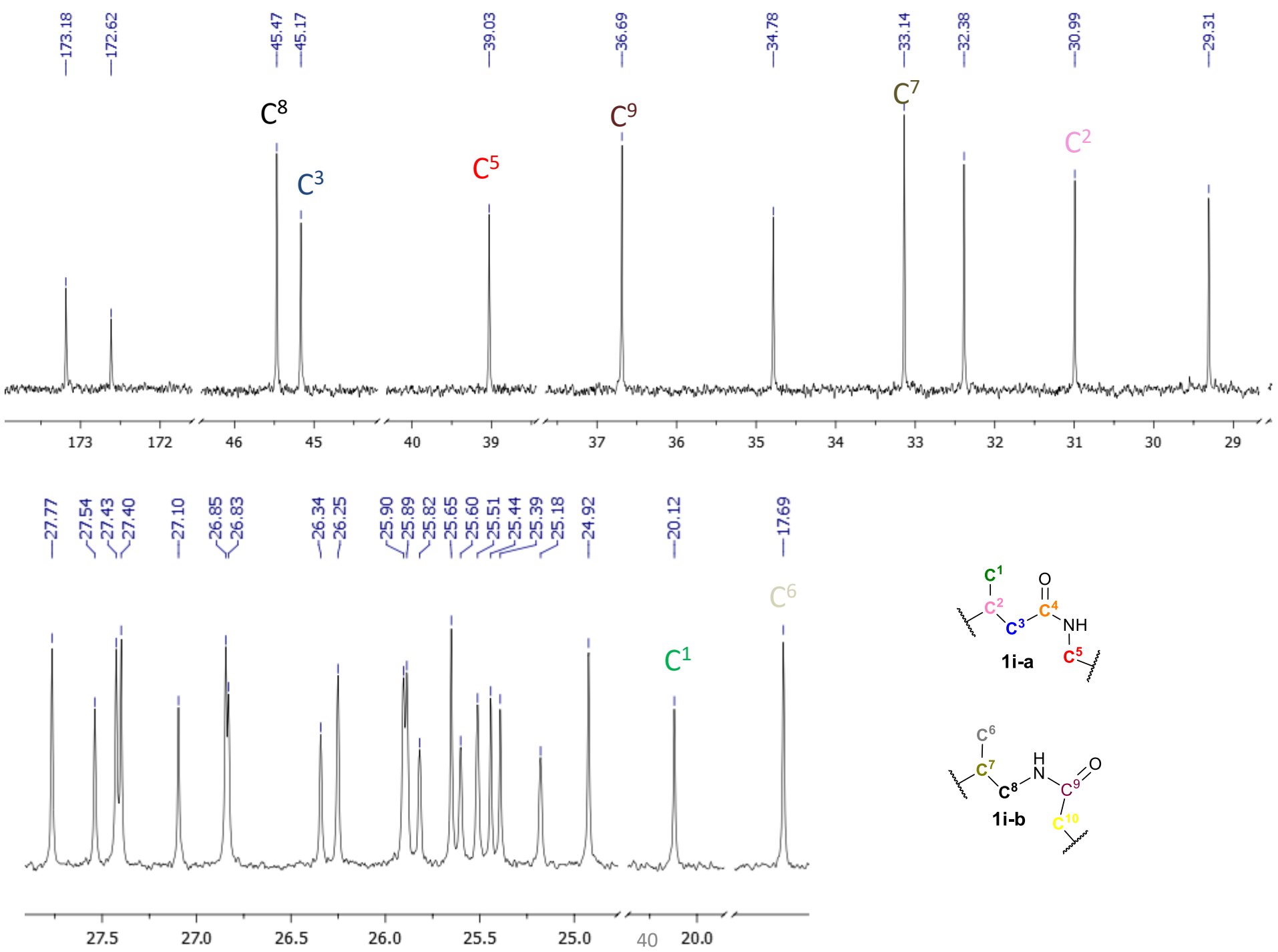
^{1}H NMR (600 MHz, Chloroform-*d*)

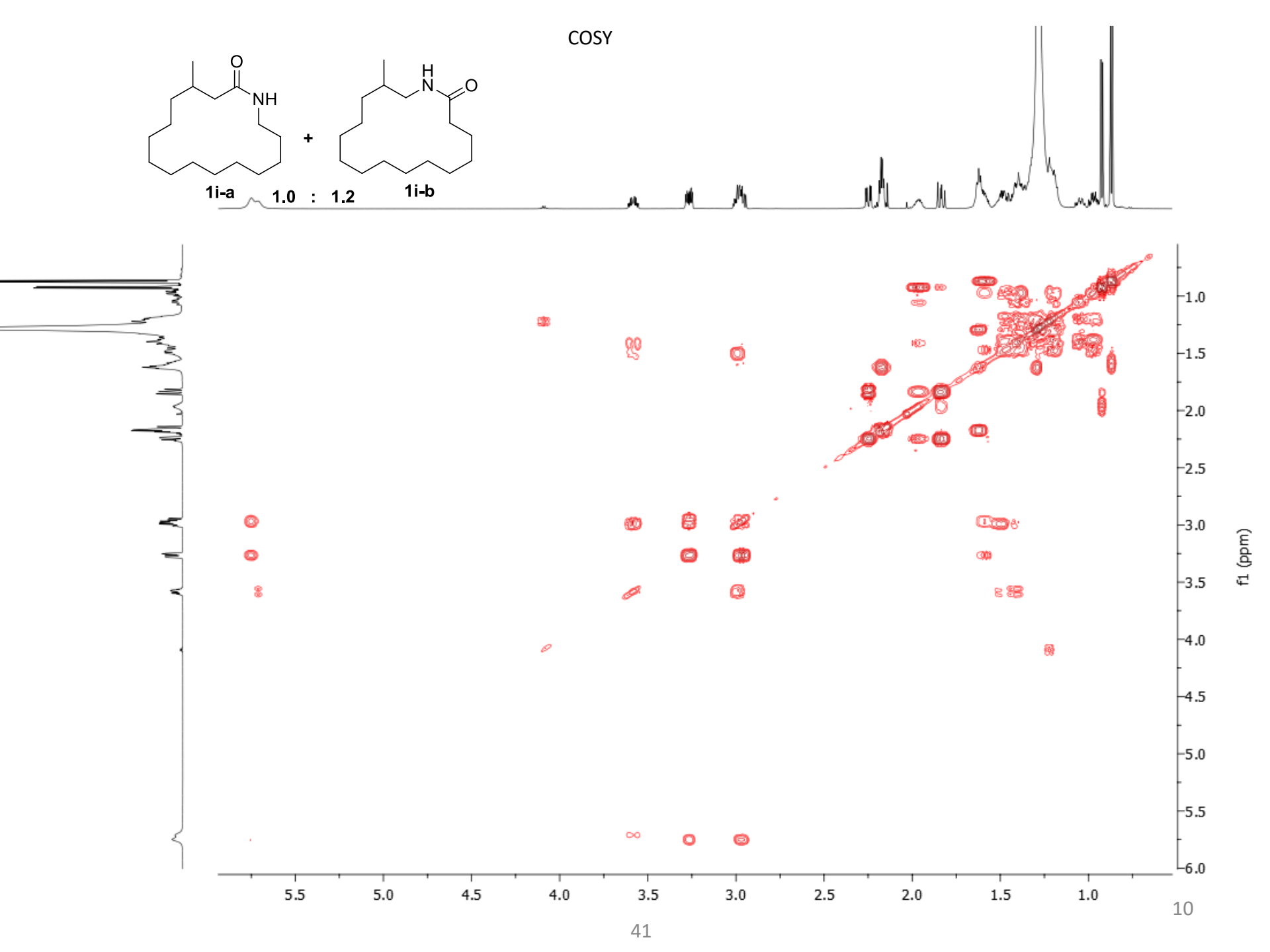



5.75
5.71
3.60
3.60
3.59
3.59
3.59
3.58
3.58
3.57
3.56
3.28
3.28
3.27
3.26
3.26
3.25
3.25
2.99
2.98
2.98
2.97
2.97
2.96
2.95
2.94
2.26
2.23
2.19
2.18
2.18
2.17
2.17
2.16
1.96
1.86
1.84
1.83
1.82
H13
H6
H1
H8
H9, H2
H3
H11, H12
H5
H4
1.22
1.01
1.00
1.22
2.01
1.02
2.18
1.10
0.90
5.80
5.75
5.70
5.65
3.65
3.60
3.55
3.30
3.25
3.00
2.95
2.25
2.20
2.15
2.00
1.95
1.90
1.85
1.80
1.63
1.62
1.61
0.93
0.92
0.88
0.86
H7
CH3
CH3
2.01
2.14
2.96
1.66
1.62
1.58
1.54
0.92
0.88
0.84
H5
CH3
O
H6
N
H3
H4
H2
H1
1i-a
H7
CH3
H13
N
O
H8
H9
H11
H12
1i-b

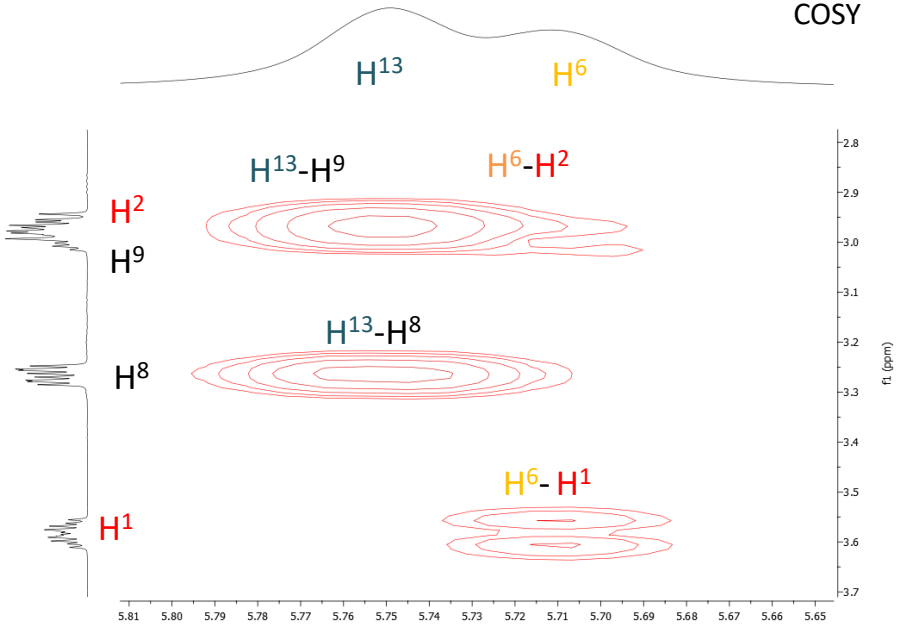
^{13}C NMR (151 MHz, Chloroform-*d*)

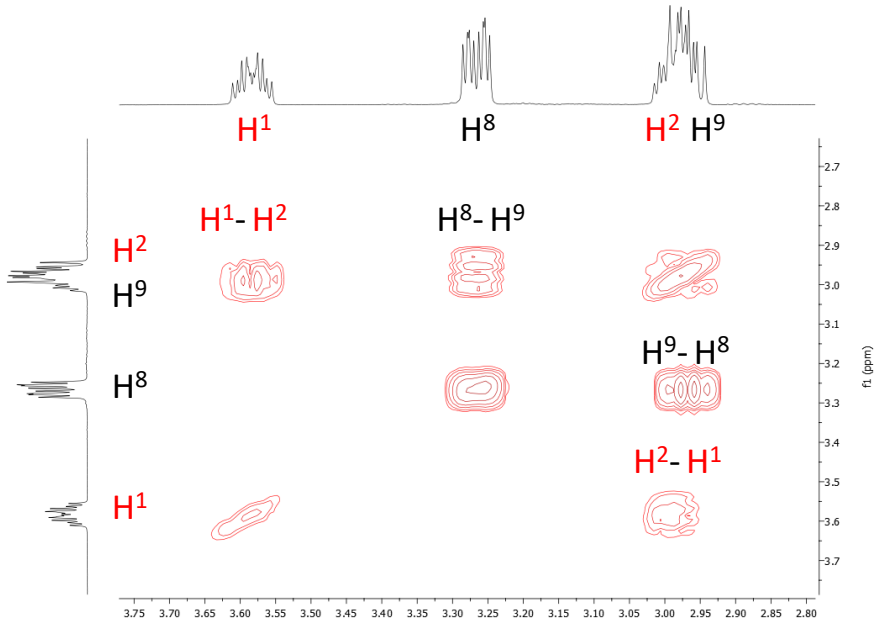


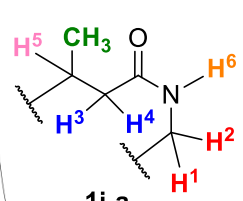

173.18
172.62
45.47
45.17
39.03
36.69
34.78
33.14
32.38
30.99
29.31
C8
C3
C5
C9
C7
C2
173
172
46
45
40
39
37
36
35
34
33
32
31
30
29
27.77
27.54
27.43
27.40
27.10
26.85
26.83
26.34
26.25
25.90
25.89
25.82
25.65
25.60
25.51
25.44
25.39
25.18
24.92
20.12
17.69
C6
C1
27.5
27.0
26.5
26.0
25.5
25.0
40
20.0
C1
C2
C3
C4
O
NH
C5
1i-a
C6
C7
C8
H
N
C9
O
C10
1i-b


COSY
O
NH
+
H
N
O
1i-a
1.0 : 1.2
1i-b
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
f1 (ppm)

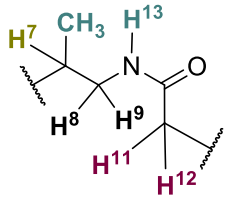
COSY


H13
H6
H13-H9
H6-H2
H2
H9
H13-H8
H8
H6- H1
H1

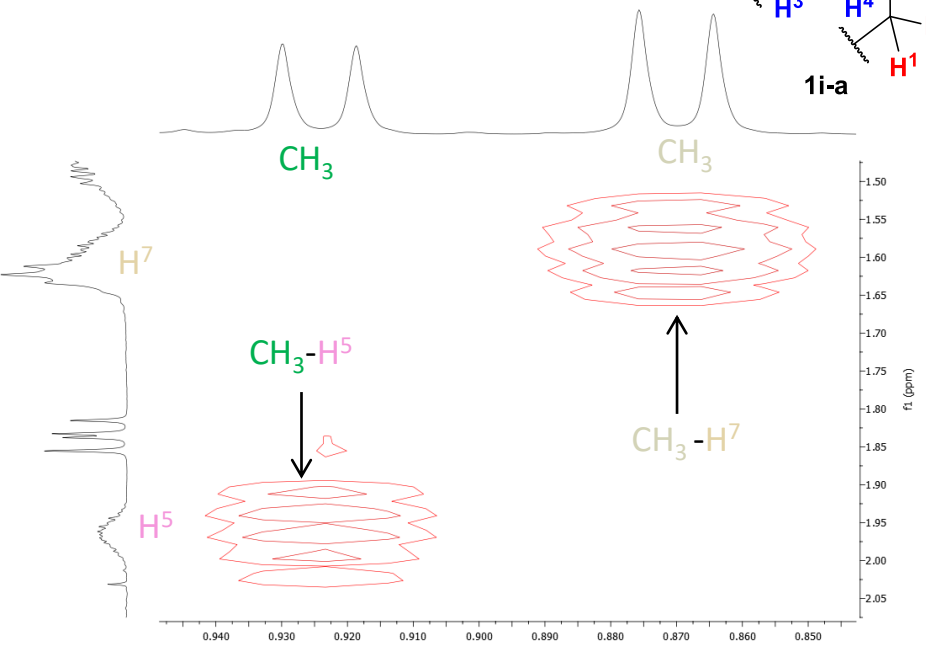

H1
H8
H2 H9
H1- H2
H8- H9
H2
H9
H9- H8
H8
H2- H1
H1

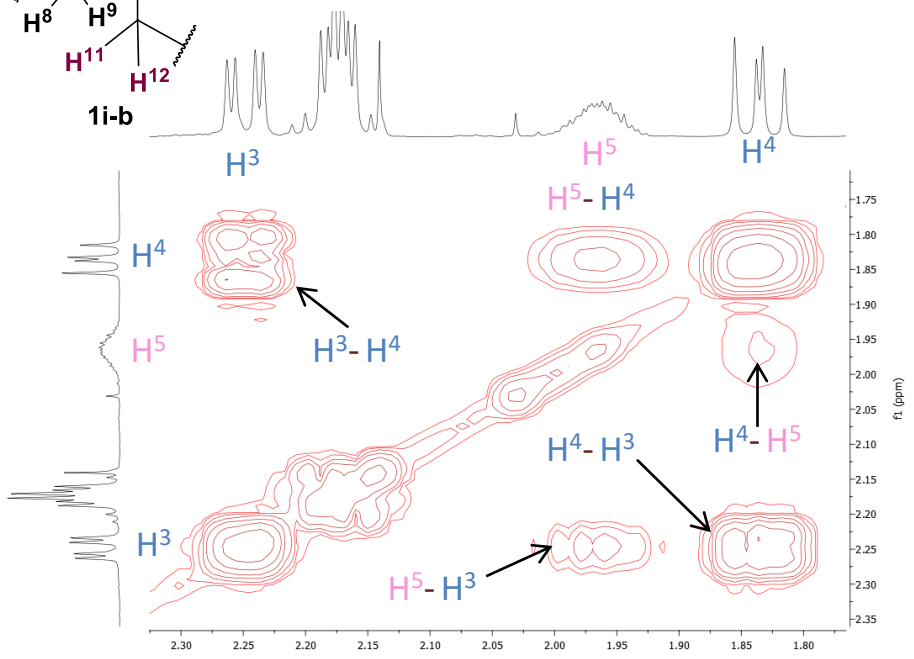

H5
CH3
O
H6
N
H3
H4
H2
H1

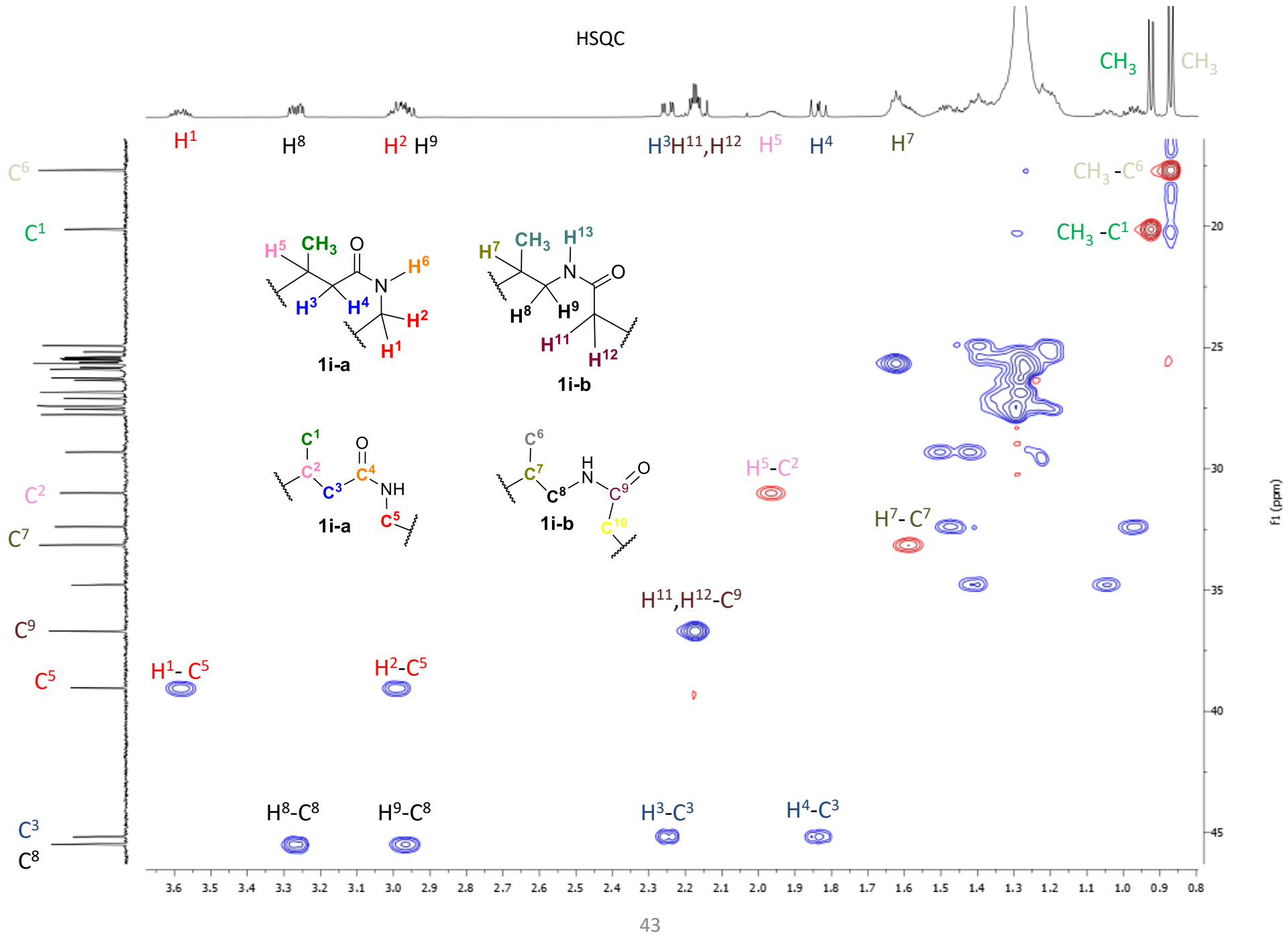
1i-a

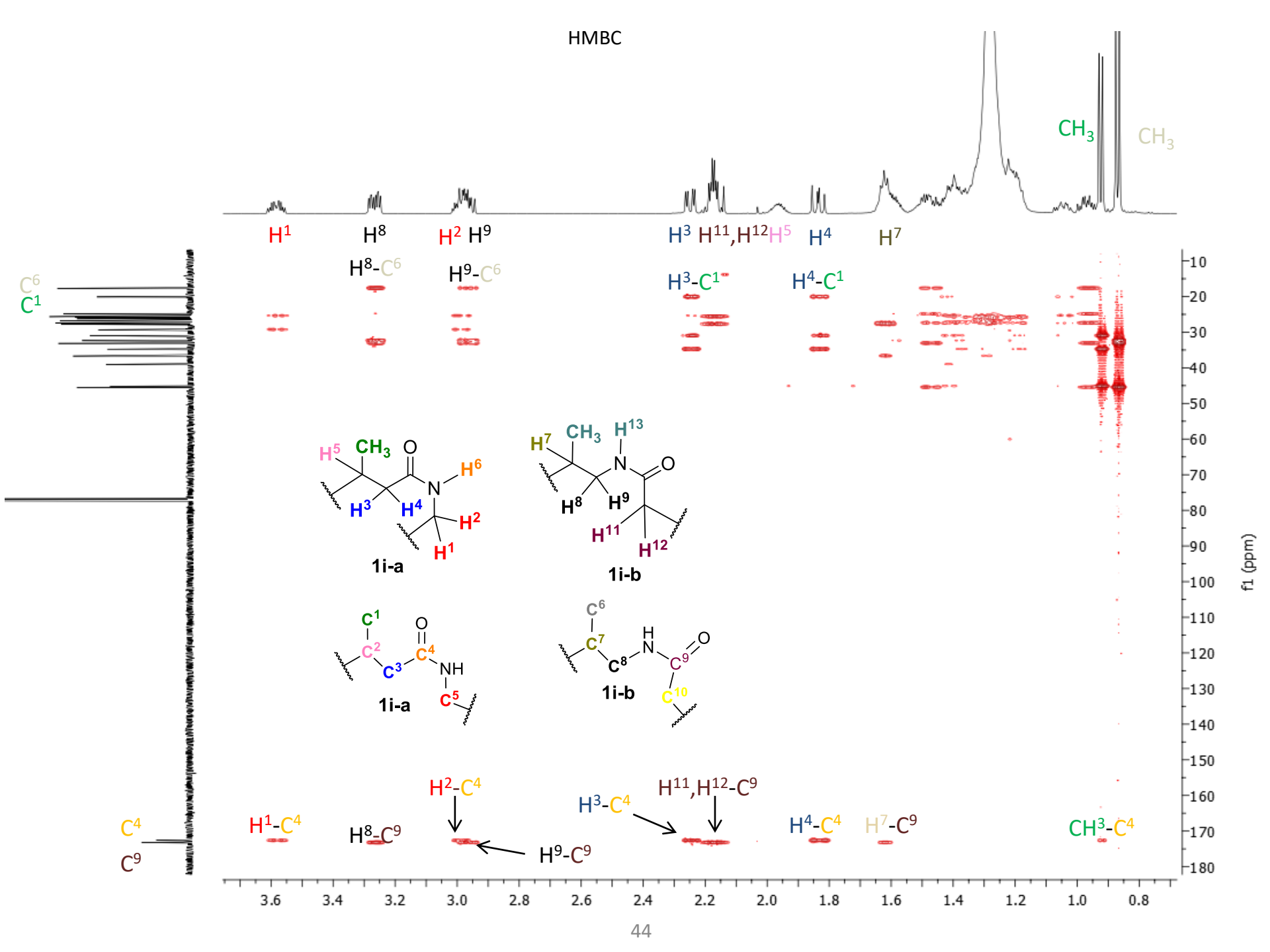

H7
CH3
H13
N
O
H8
H9
H11
H12

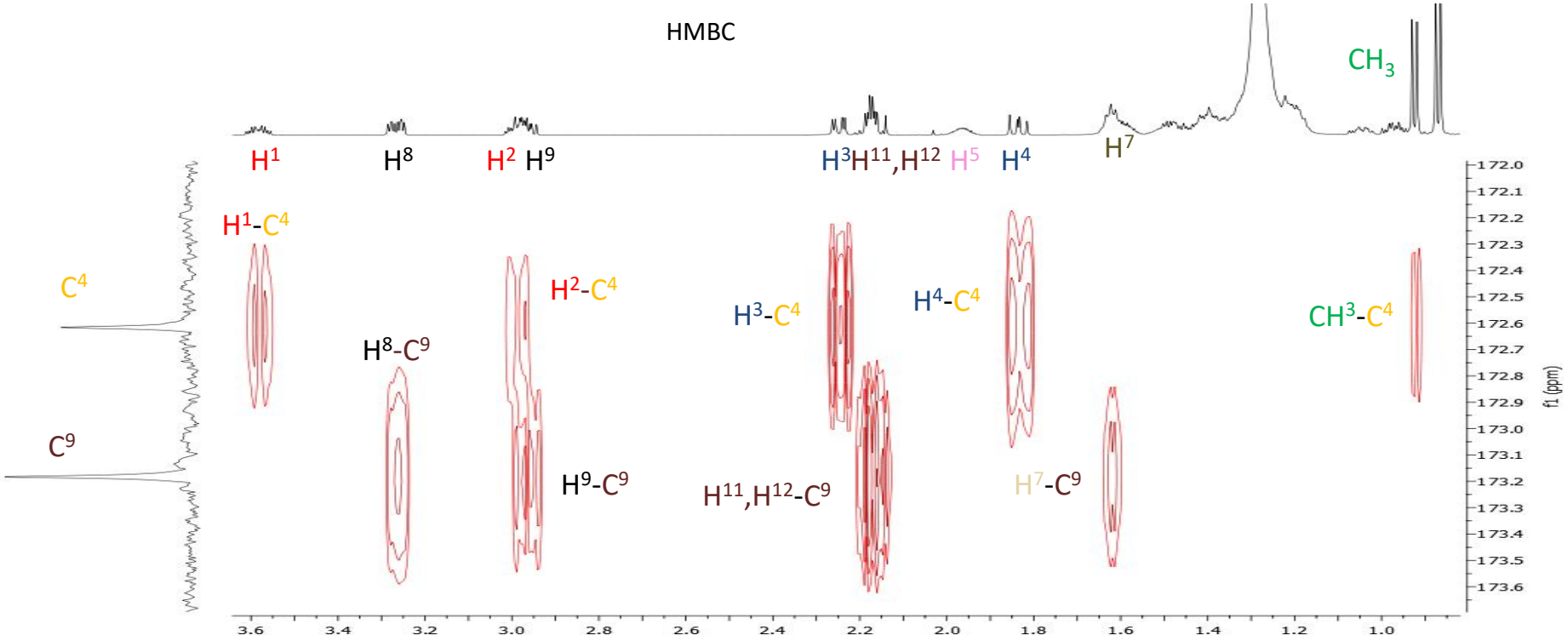
1i-b

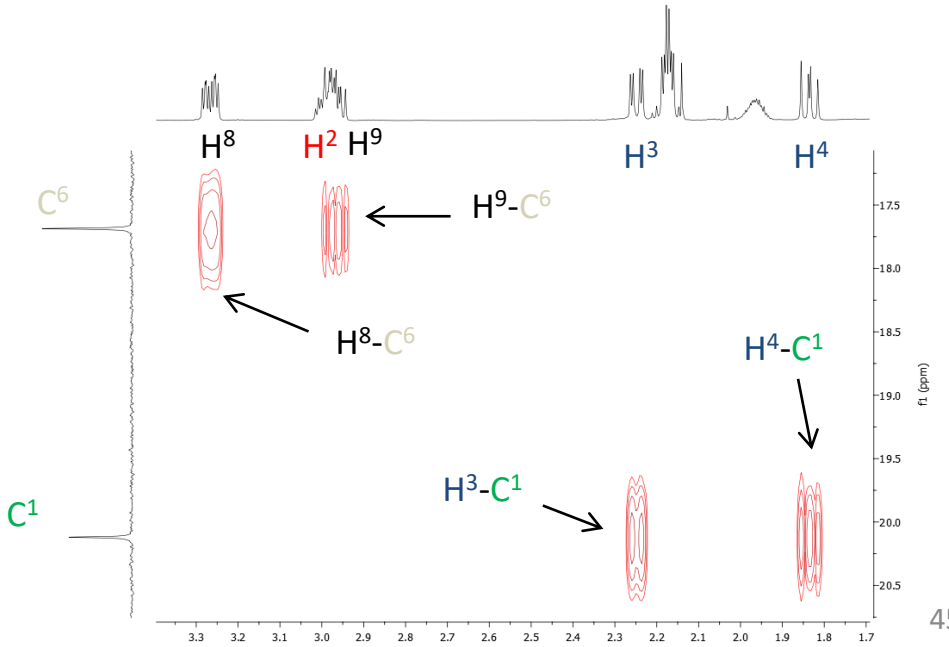

CH3
CH3
H7
CH3-H5
CH3 -H7
H5

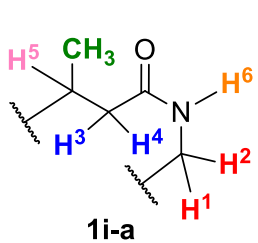

H3
H5
H4
H5- H4
H4
H3- H4
H5
H4- H3
H4- H5
H3
H5- H3


HSQC
CH3
CH3
H1
H8
H2 H9
H3H11,H12
H5
H4
H7
C6
C1
C2
C7
C9
C5
C3
C8
CH3 -C6
CH3 -C1
H5 CH3 O H6 H3 H4 H2 H1
1i-a
H7 CH3 H13 N O H8 H9 H11 H12
1i-b
C1 C2 C3 C4 O NH C5
1i-a
C6 C7 C8 N C9 C10 O H
1i-b
H5-C2
H7- C7
H11,H12-C9
H1- C5
H2-C5
H8-C8
H9-C8
H3-C3
H4-C3
20
25
30
35
40
45
F1 (ppm)
3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8

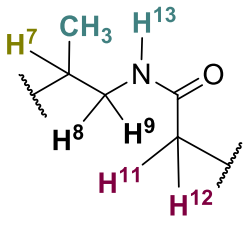

HMBC
CH3
CH3
H1
H8
H2 H9
H3 H11,H12 H5
H4
H7
H8-C6
H9-C6
H3-C1
H4-C1
C6
C1
C4
C9
1i-a
1i-b
1i-a
1i-b
H1-C4
H8-C9
H2-C4
H9-C9
H3-C4
H11,H12-C9
H4-C4
H7-C9
CH3-C4
f1 (ppm)
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8



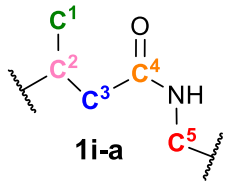




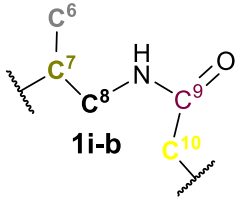
1i-a



1i-b

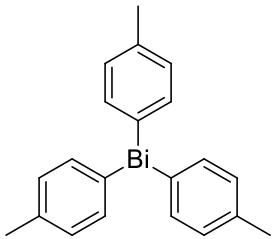


1i-a



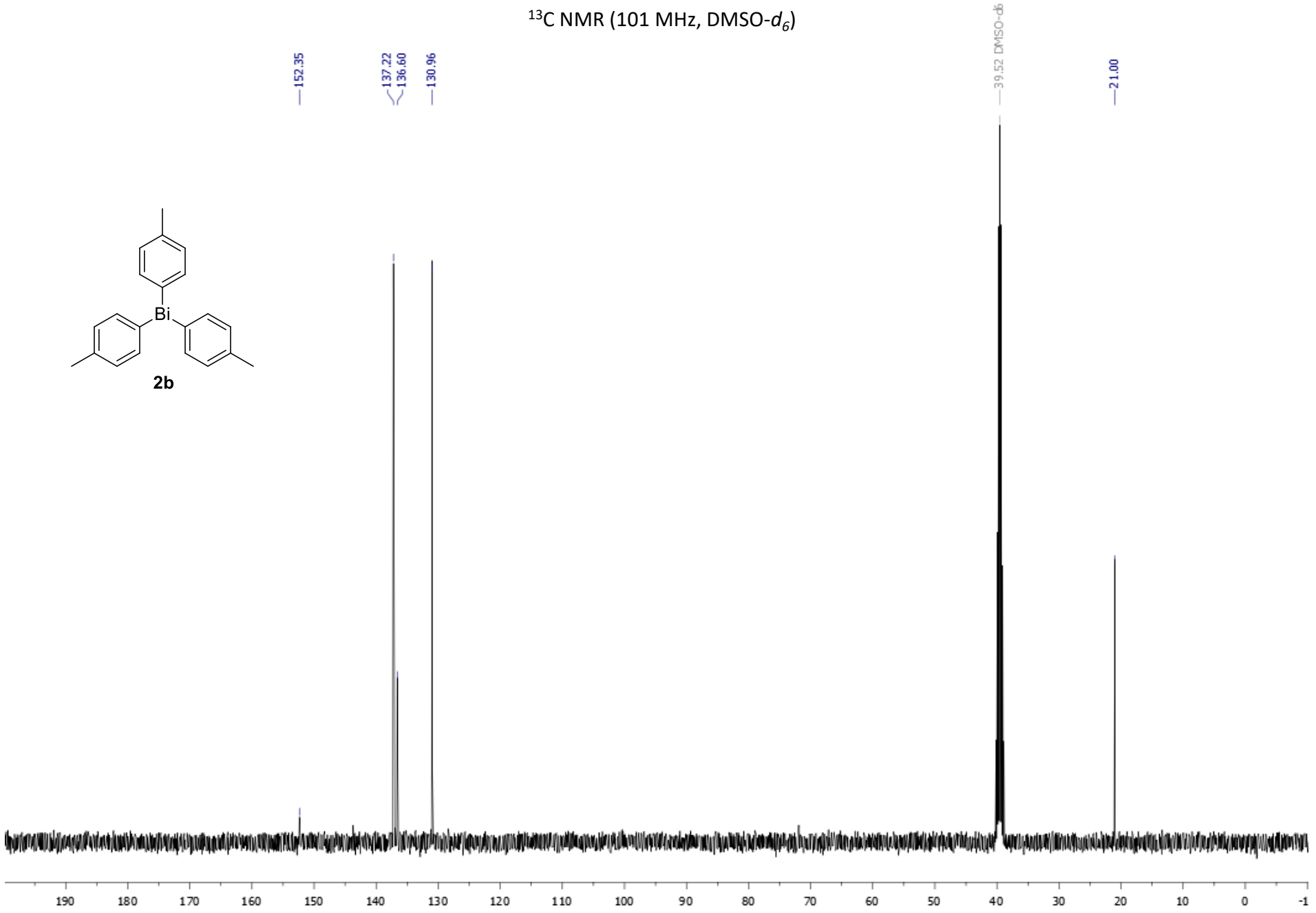
1i-b

^{1}H NMR (400 MHz, DMSO-d_6)

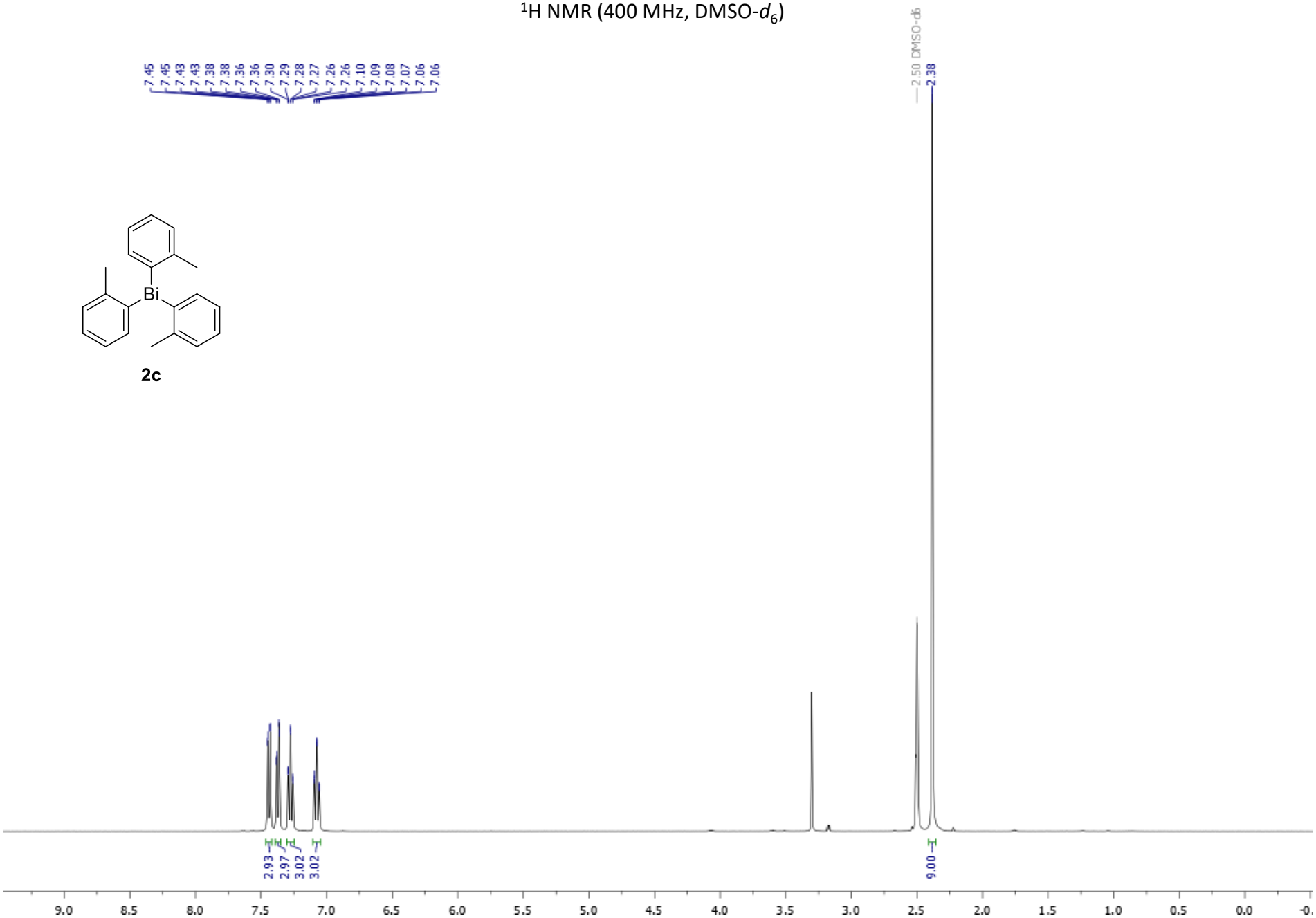


2b

^{13}C NMR (101 MHz, DMSO-d_6)

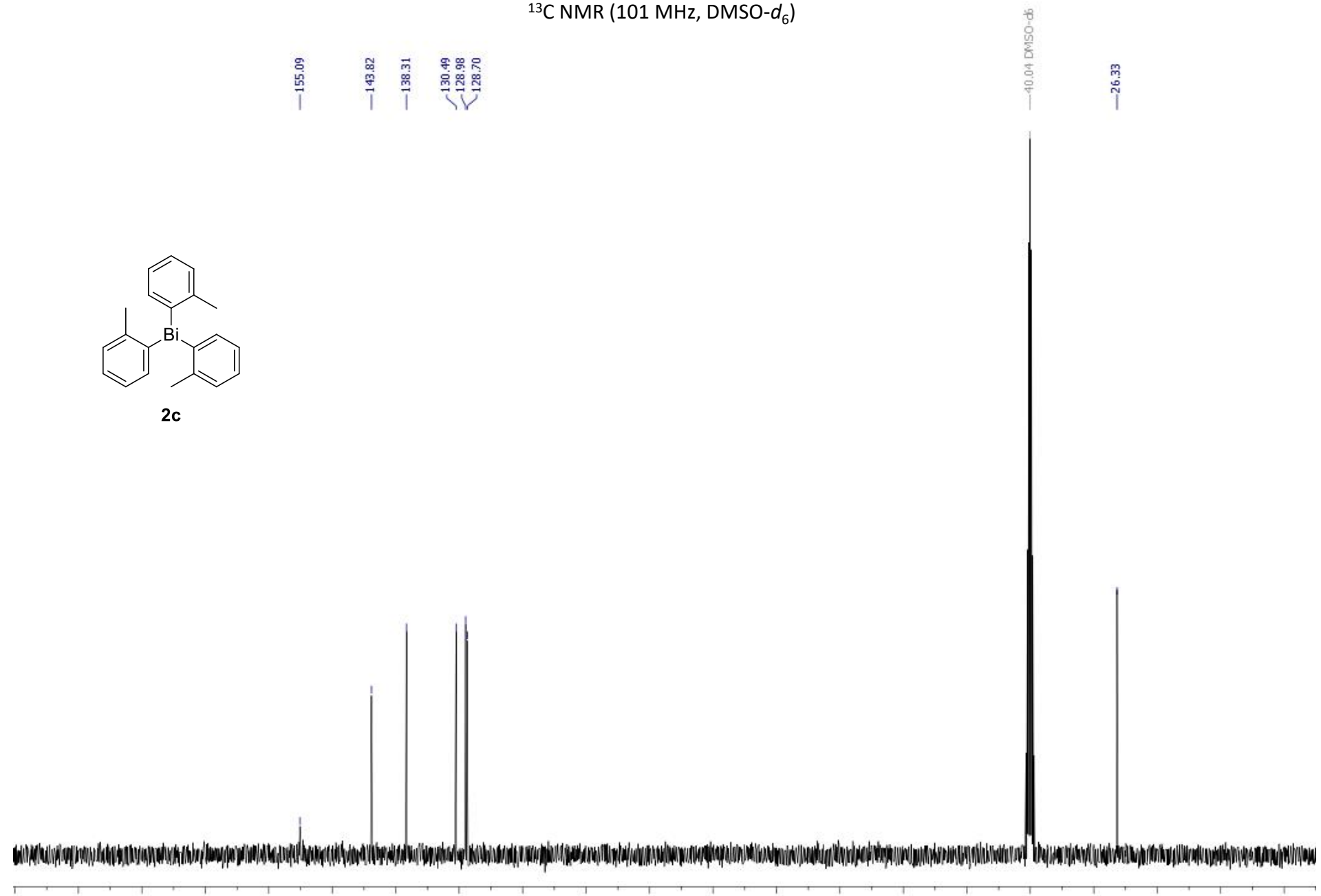


^{1}H NMR (400 MHz, DMSO-d_6)

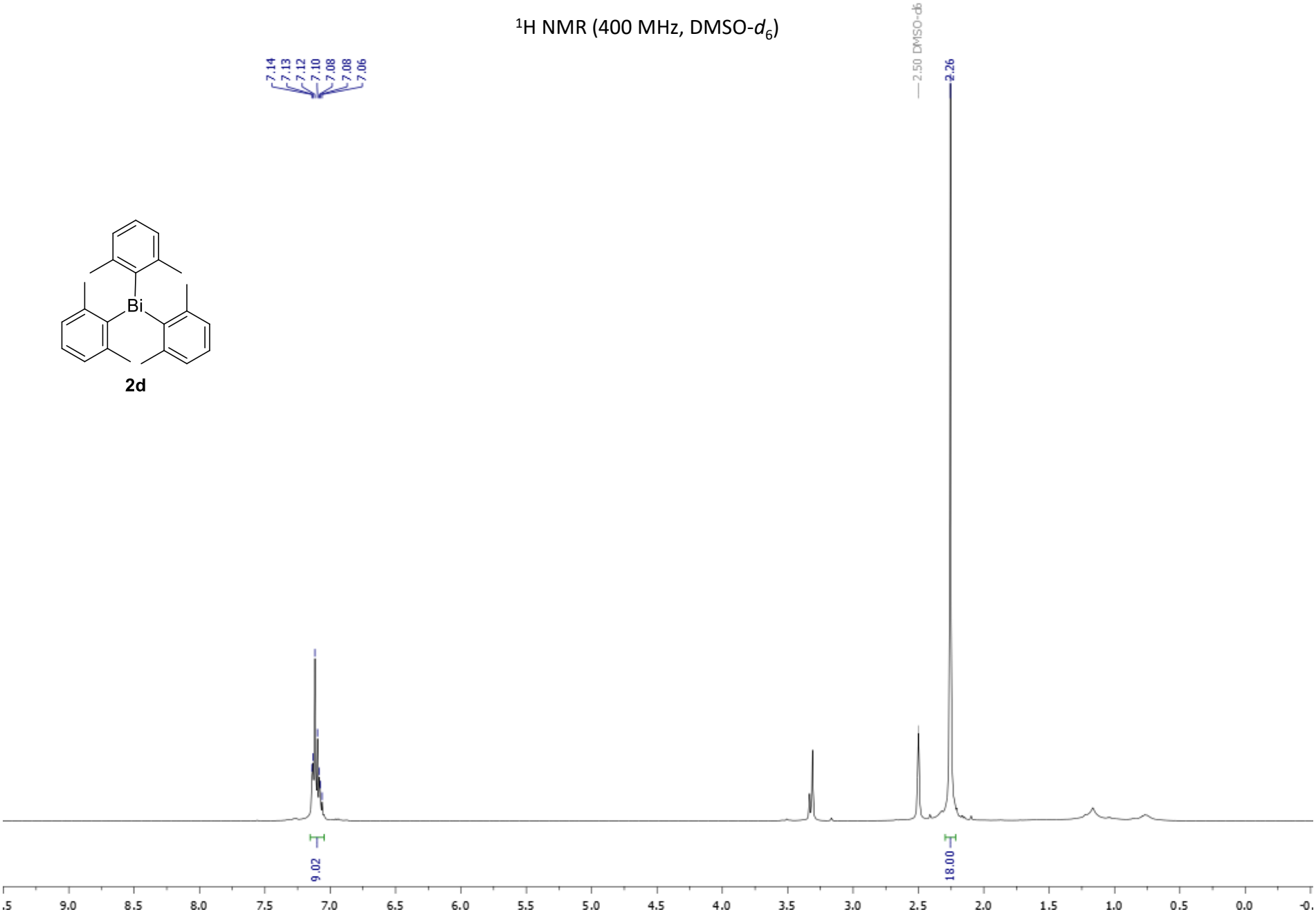


2c

^{13}C NMR (101 MHz, DMSO-d_6)

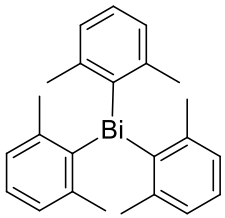


^{1}H NMR (400 MHz, DMSO-d_6)



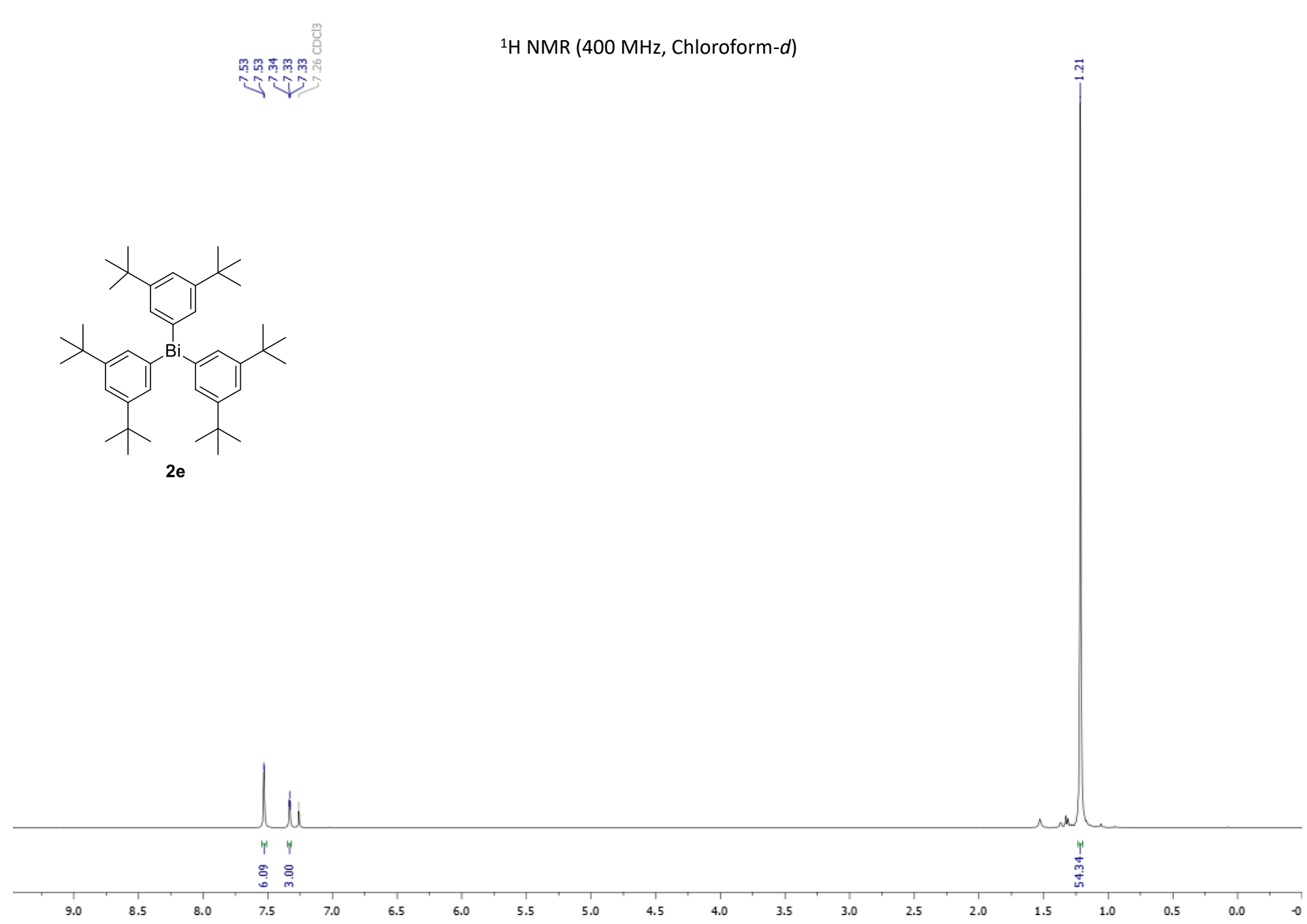
2d

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



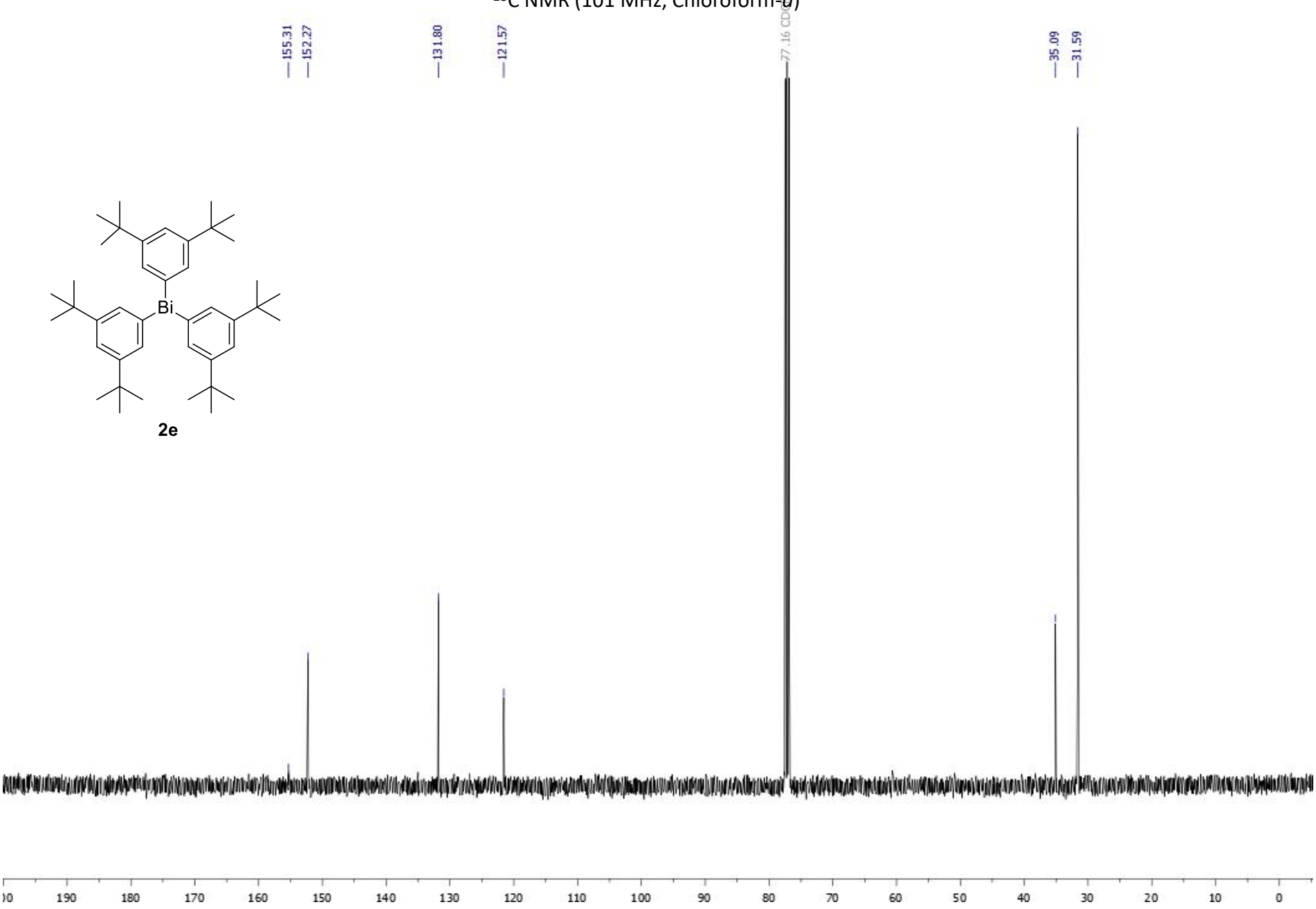
2d

^{1}H NMR (400 MHz, Chloroform-*d*)

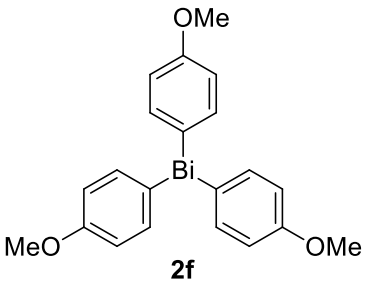


2e

^{13}C NMR (101 MHz, Chloroform-*d*)

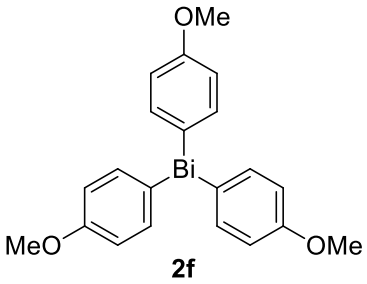


^{1}H NMR (400 MHz, DMSO-d_6)



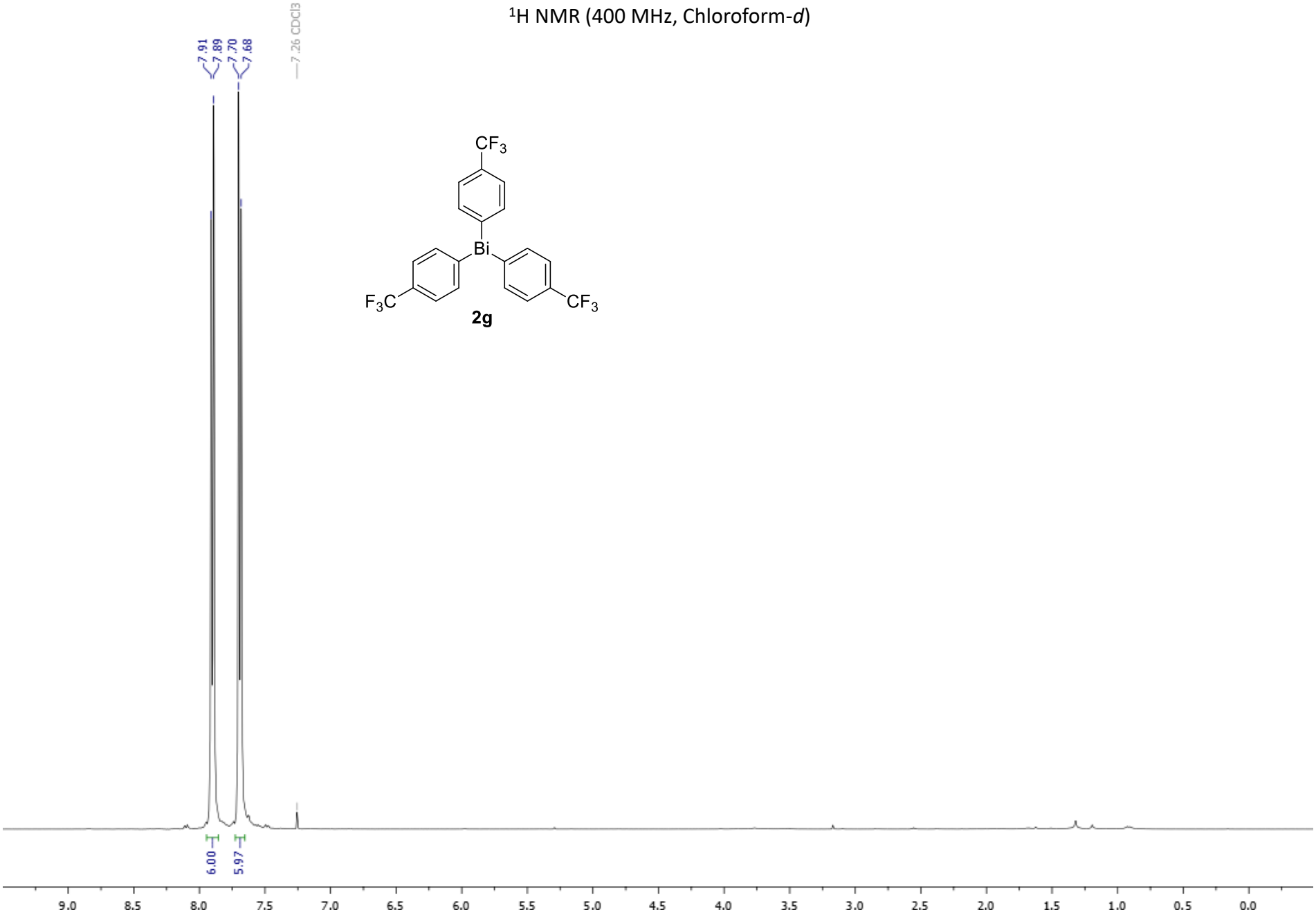
2f

^{13}C NMR (101 MHz, DMSO-d_6)



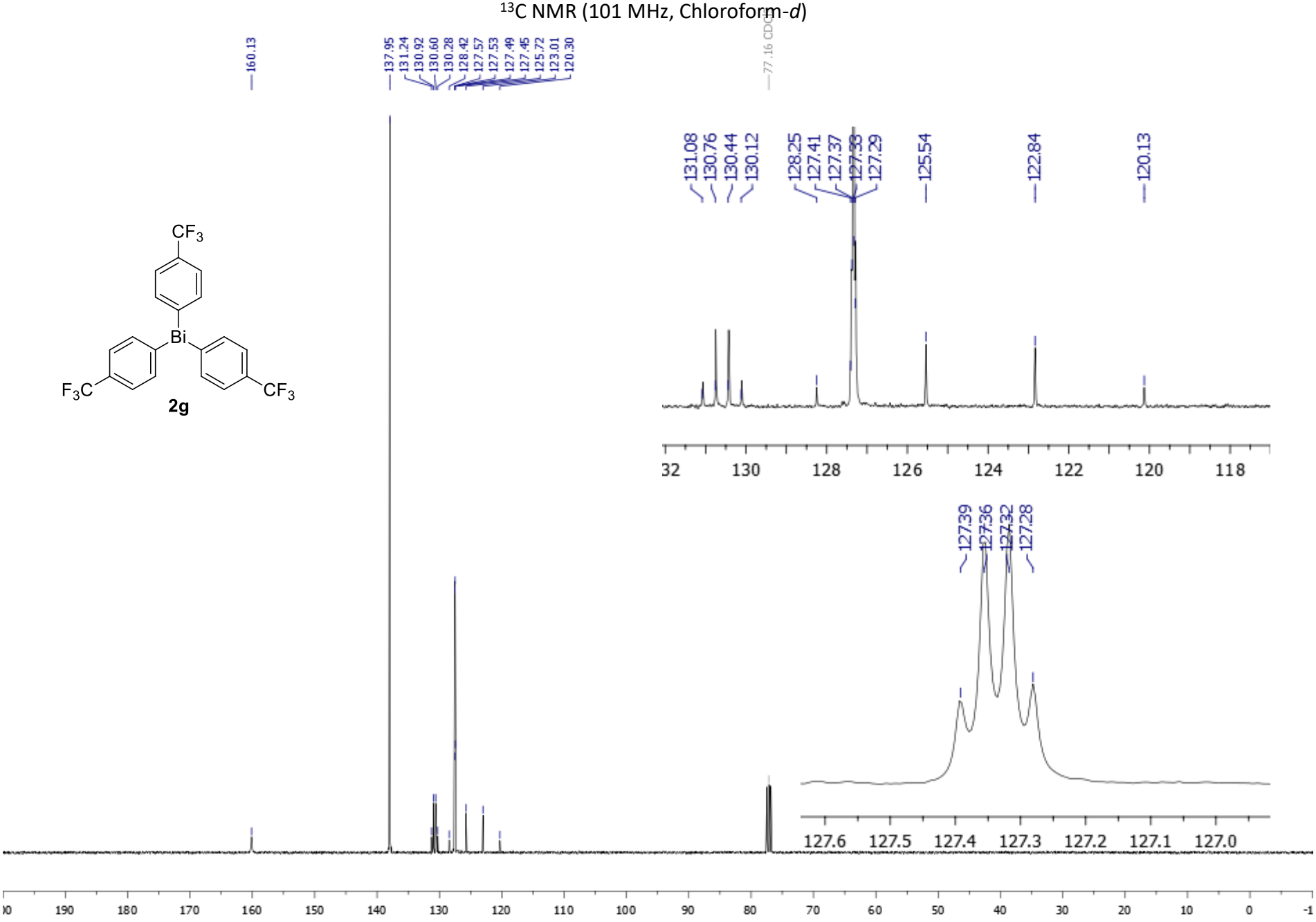
2f

^{1}H NMR (400 MHz, Chloroform-*d*)



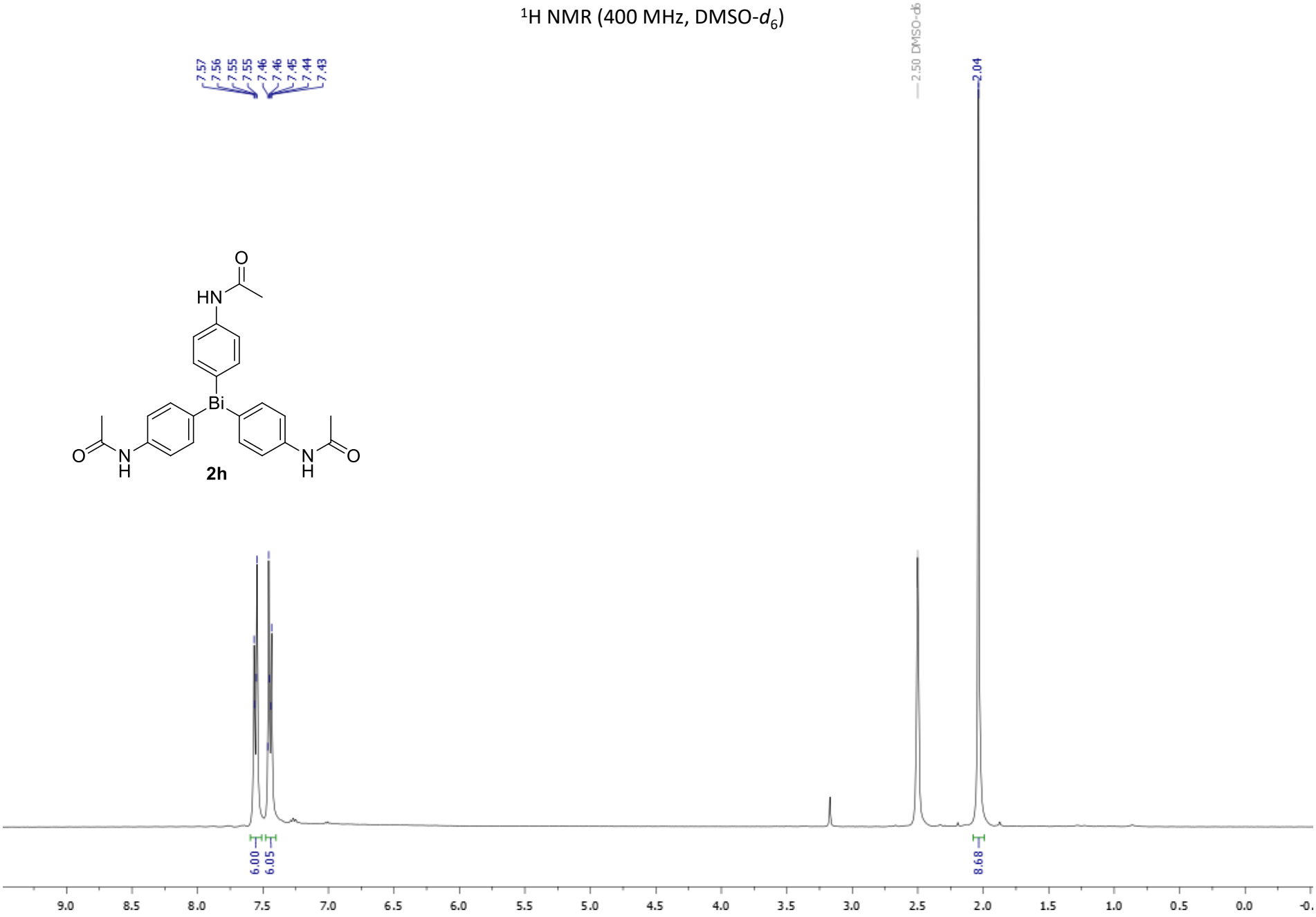
2g

^{13}C NMR (101 MHz, Chloroform-*d*)



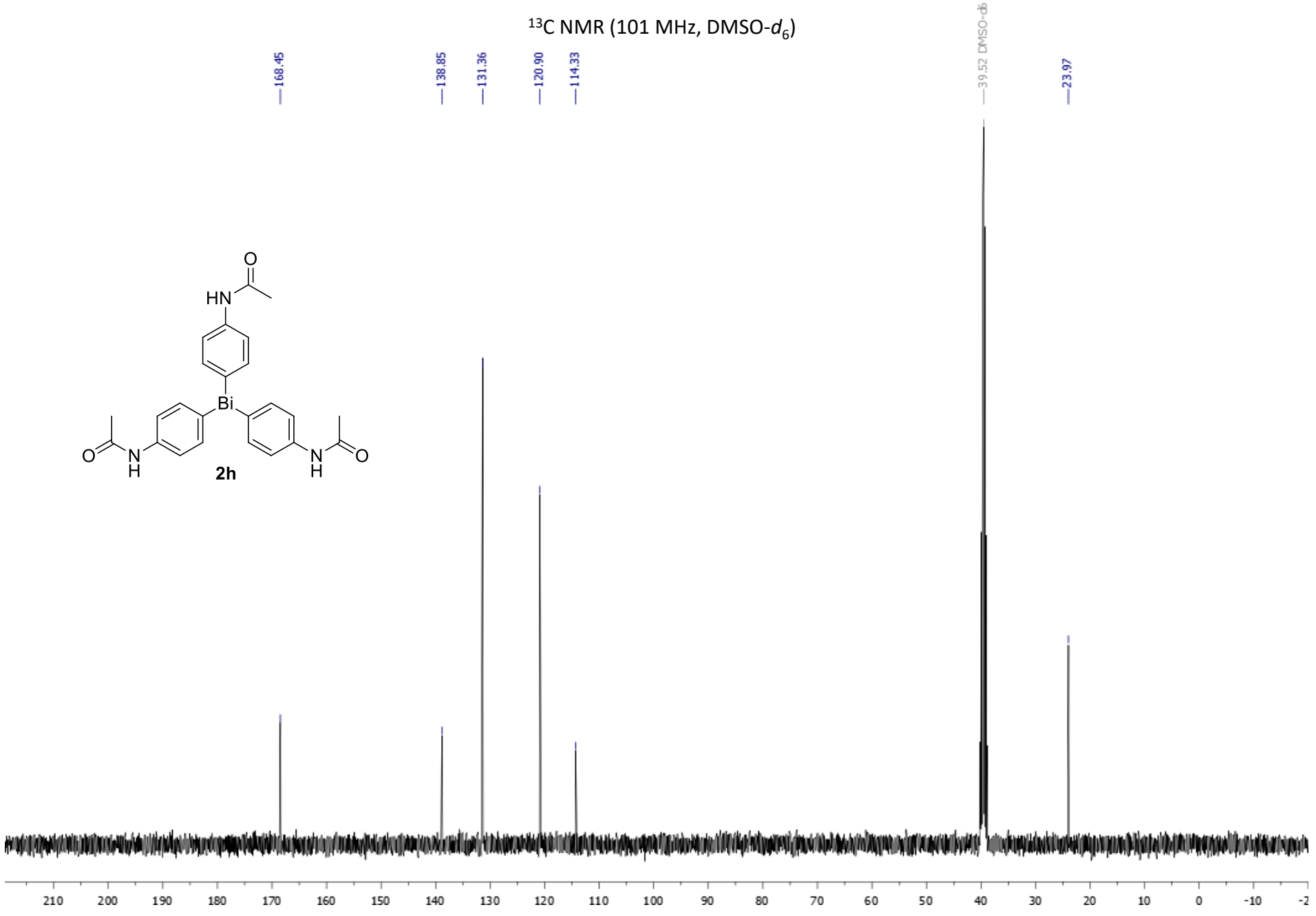
2g

^{1}H NMR (400 MHz, DMSO-d_6)

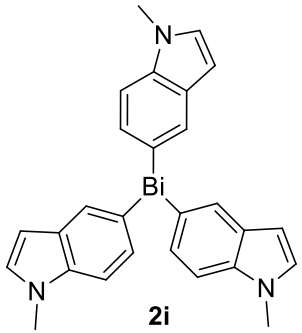


2h

^{13}C NMR (101 MHz, DMSO-d_6)

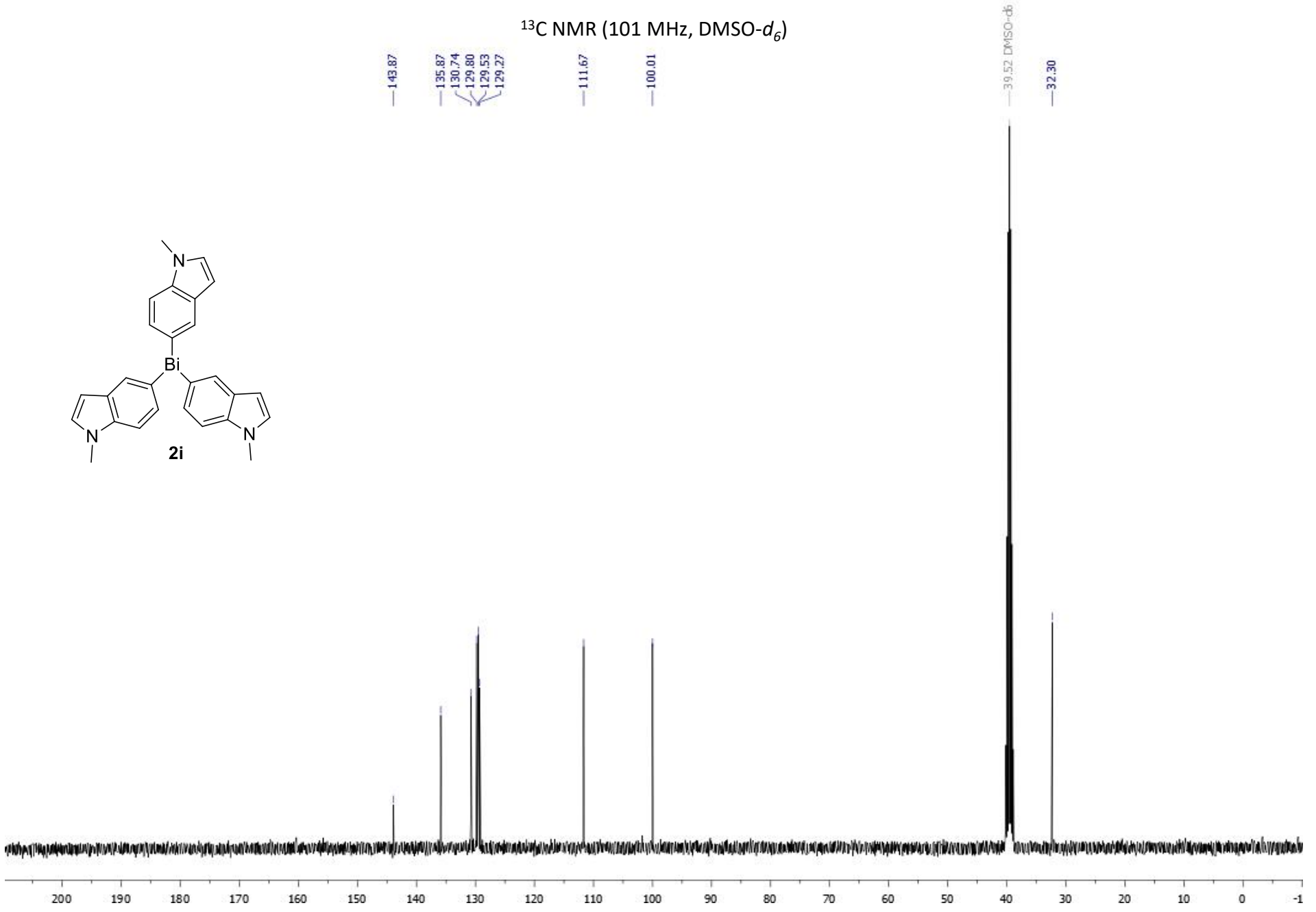


^{1}H NMR (400 MHz, DMSO-d_6)

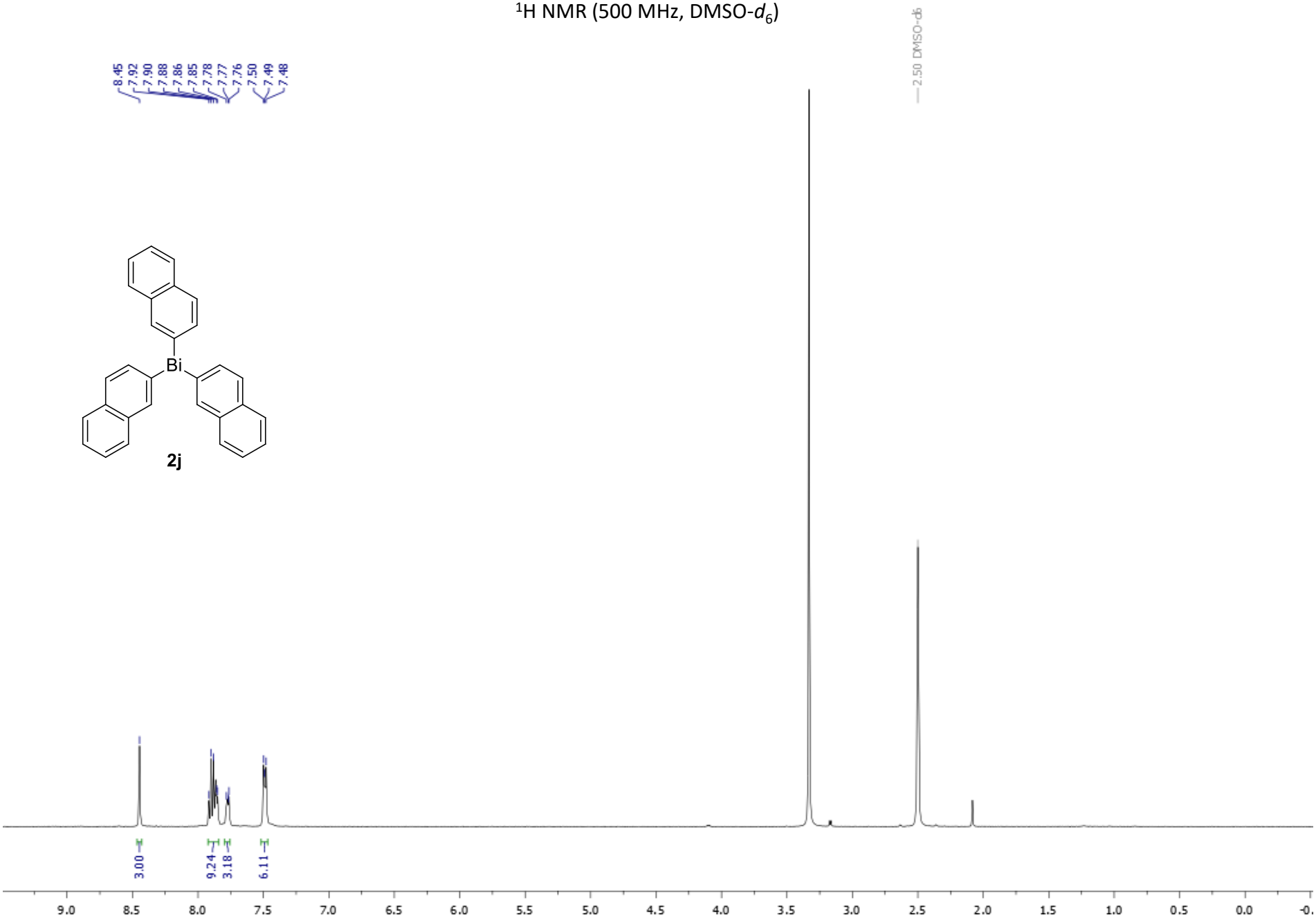


2i

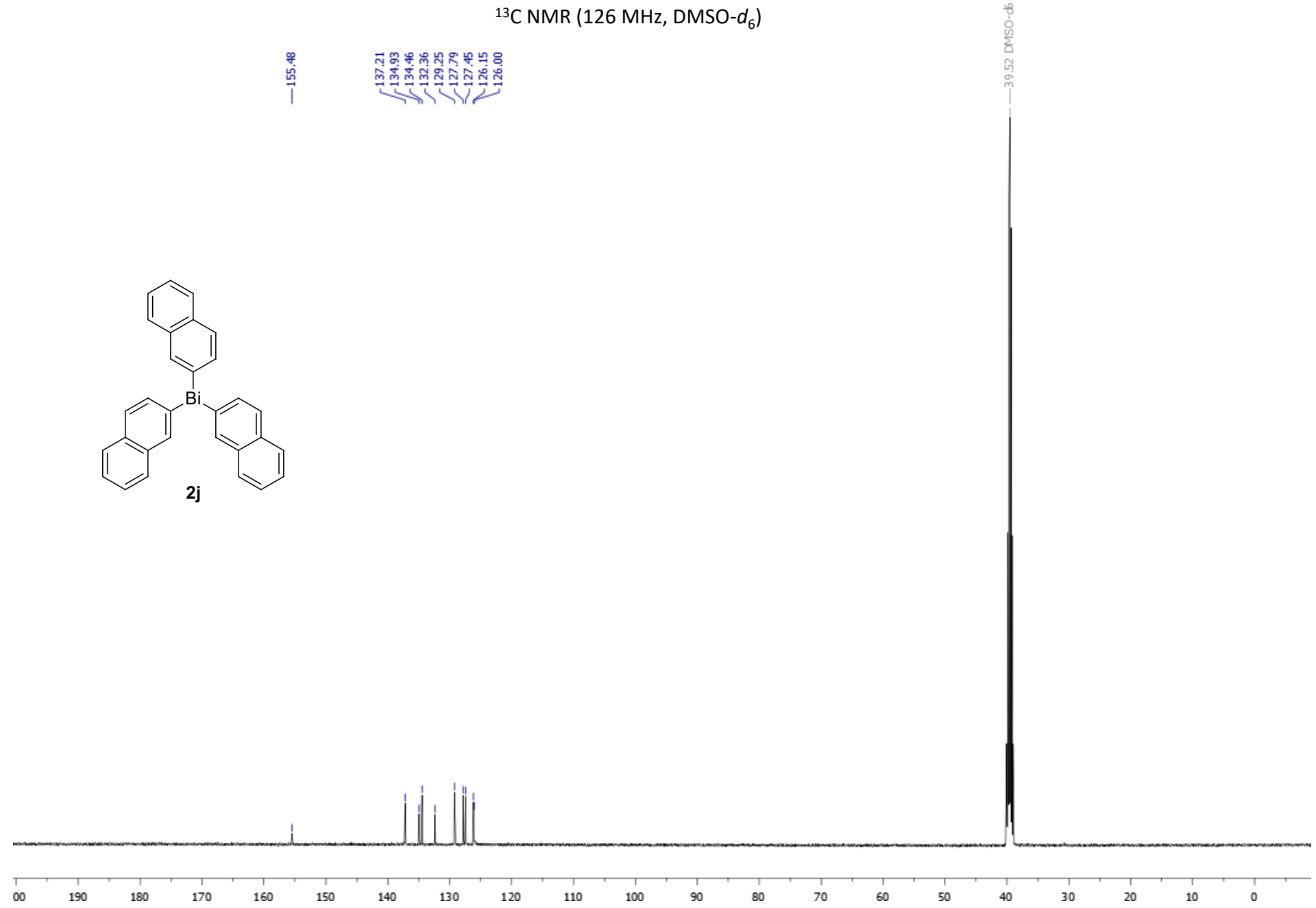
^{13}C NMR (101 MHz, DMSO-d_6)



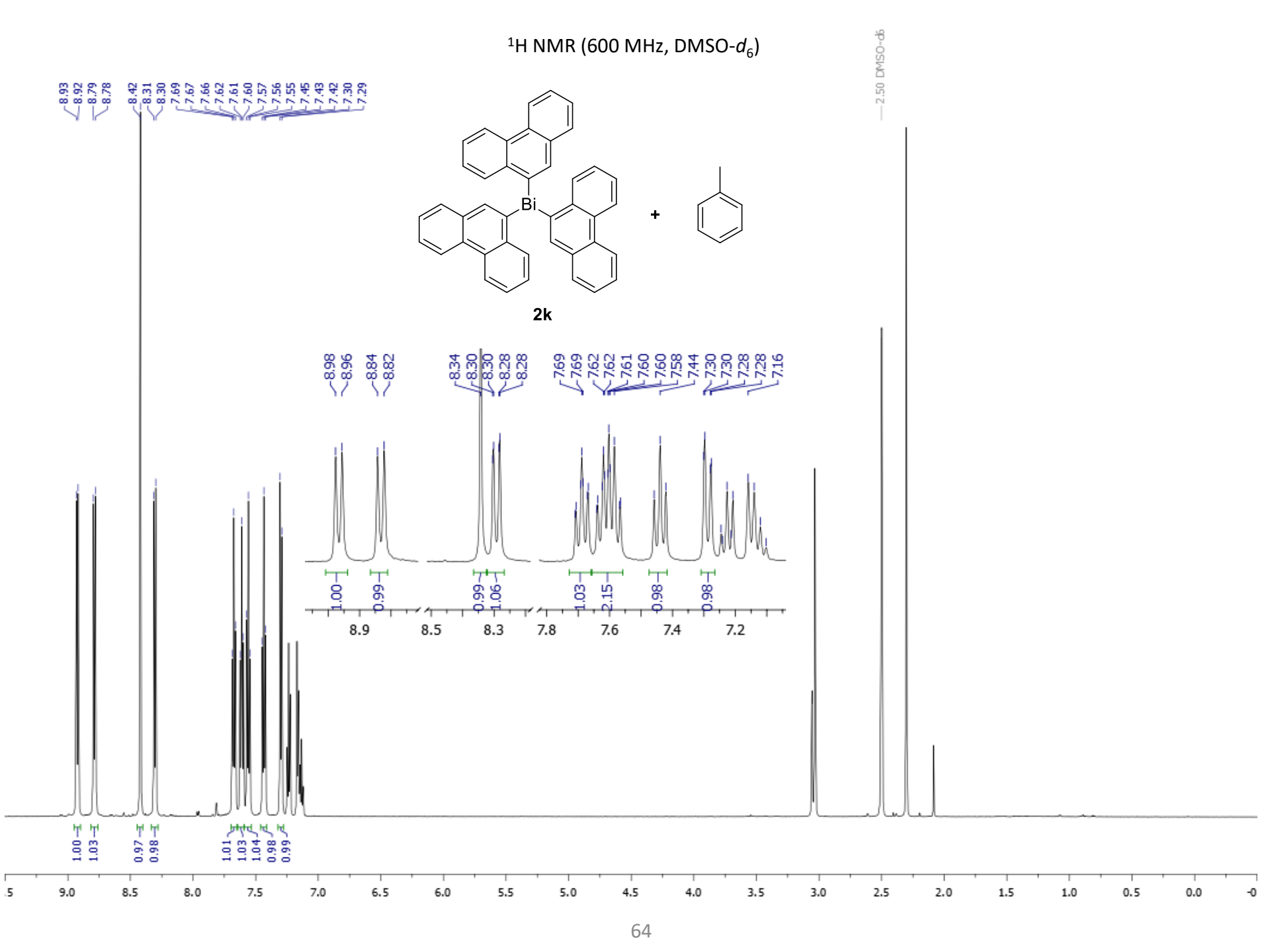
^{1}H NMR (500 MHz, DMSO-d_6)



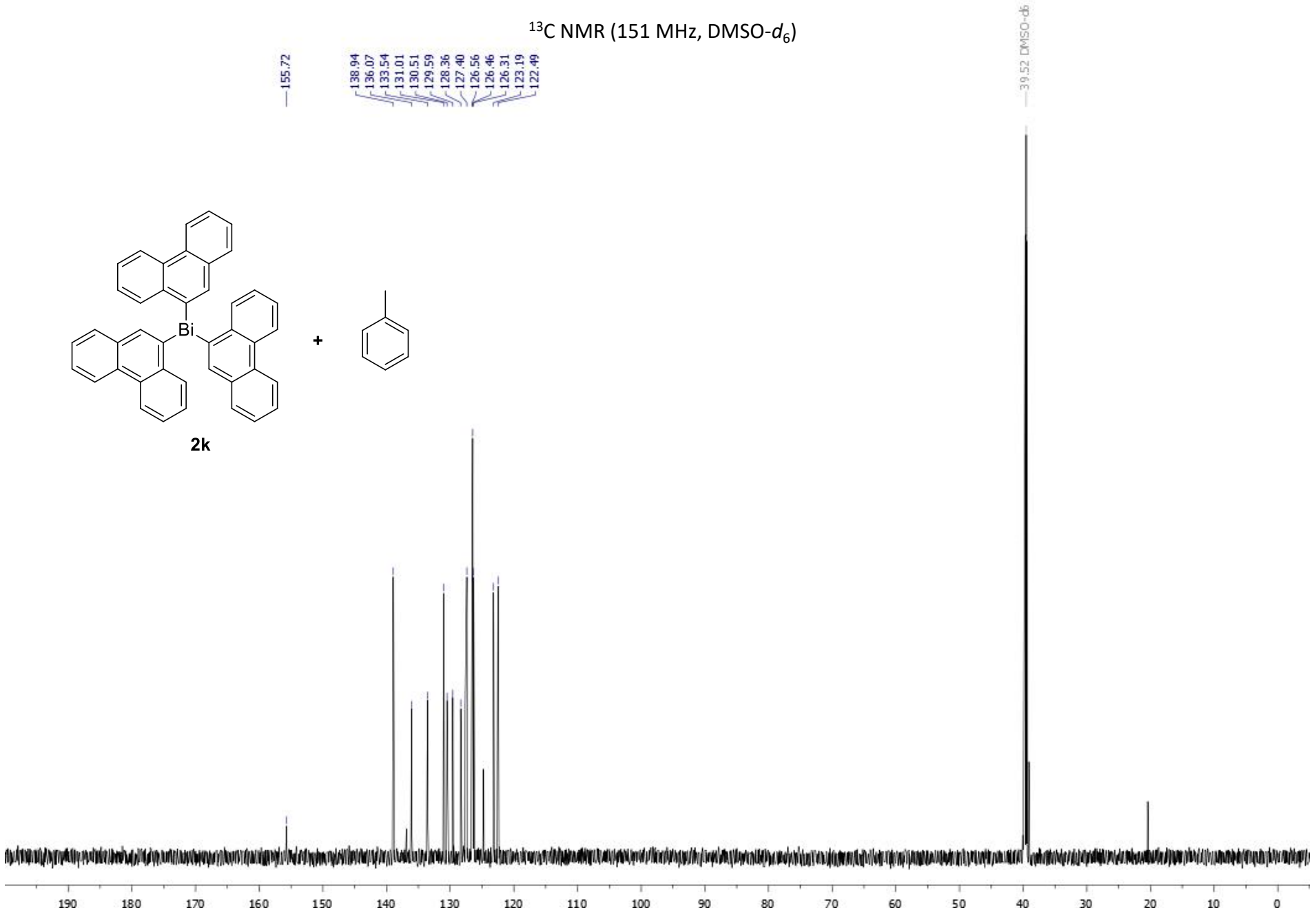
^{13}C NMR (126 MHz, DMSO-d_6)



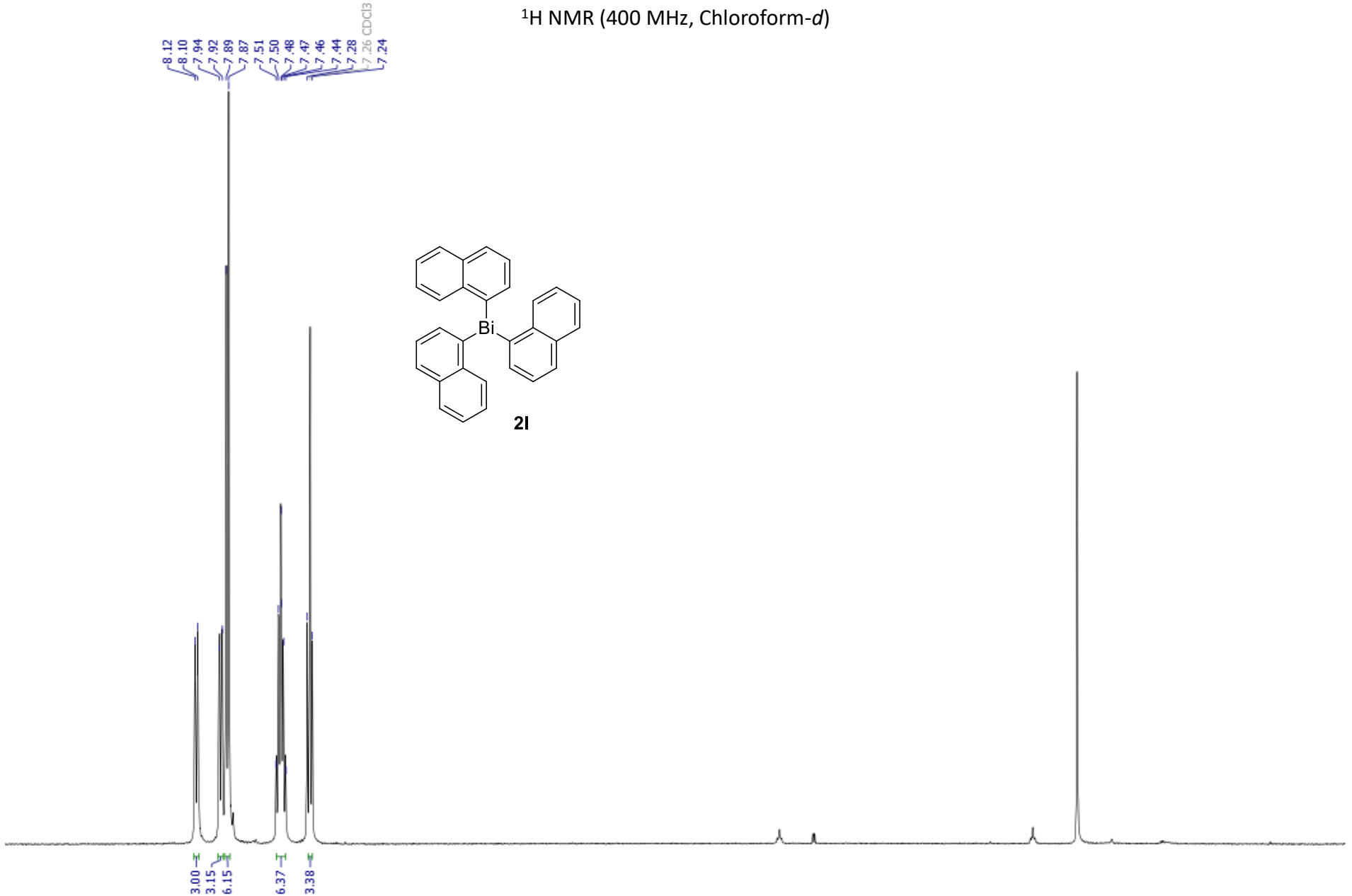
^{1}H NMR (600 MHz, DMSO-d_6)



^{13}C NMR (151 MHz, DMSO-d_6)

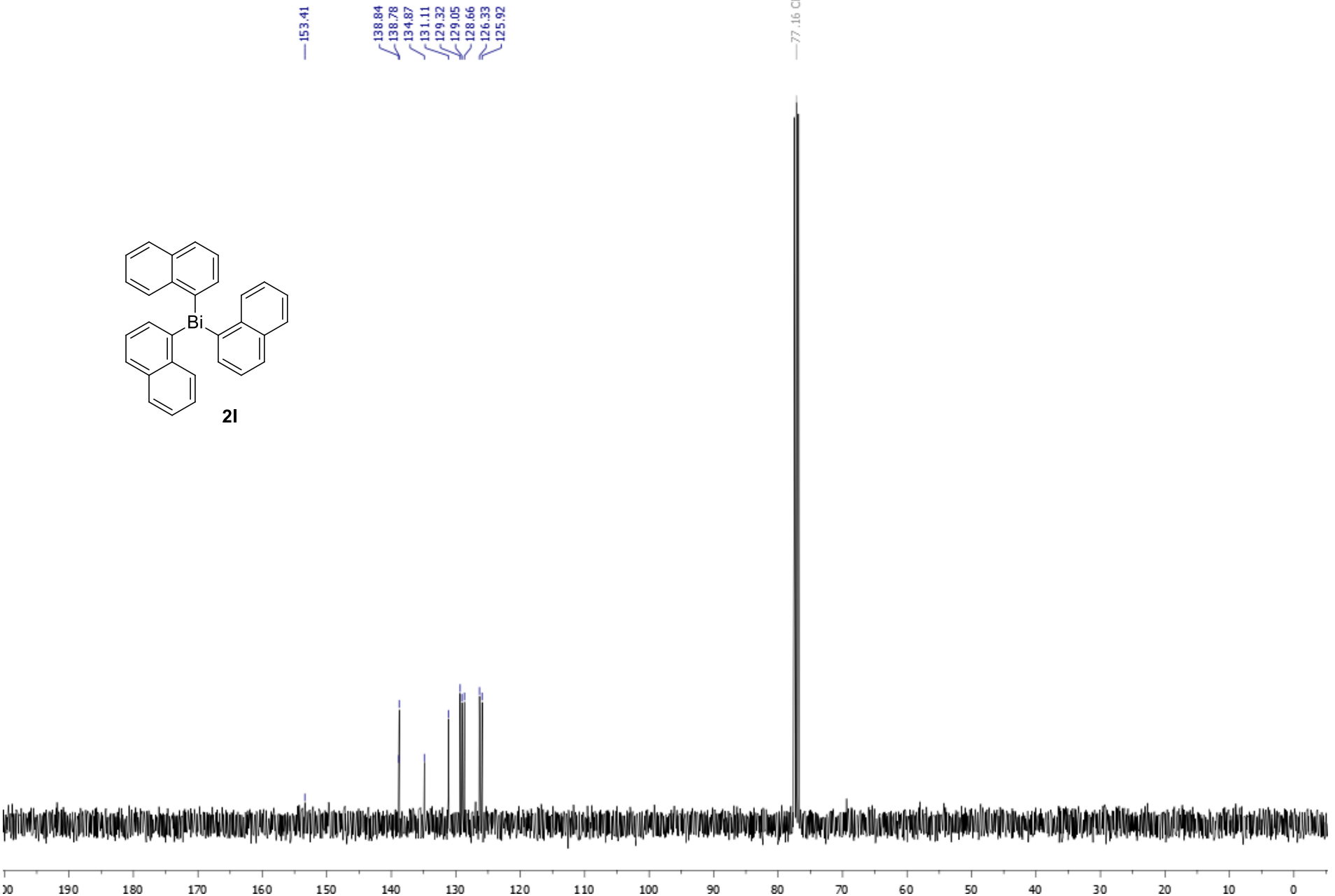


^{1}H NMR (400 MHz, Chloroform-*d*)

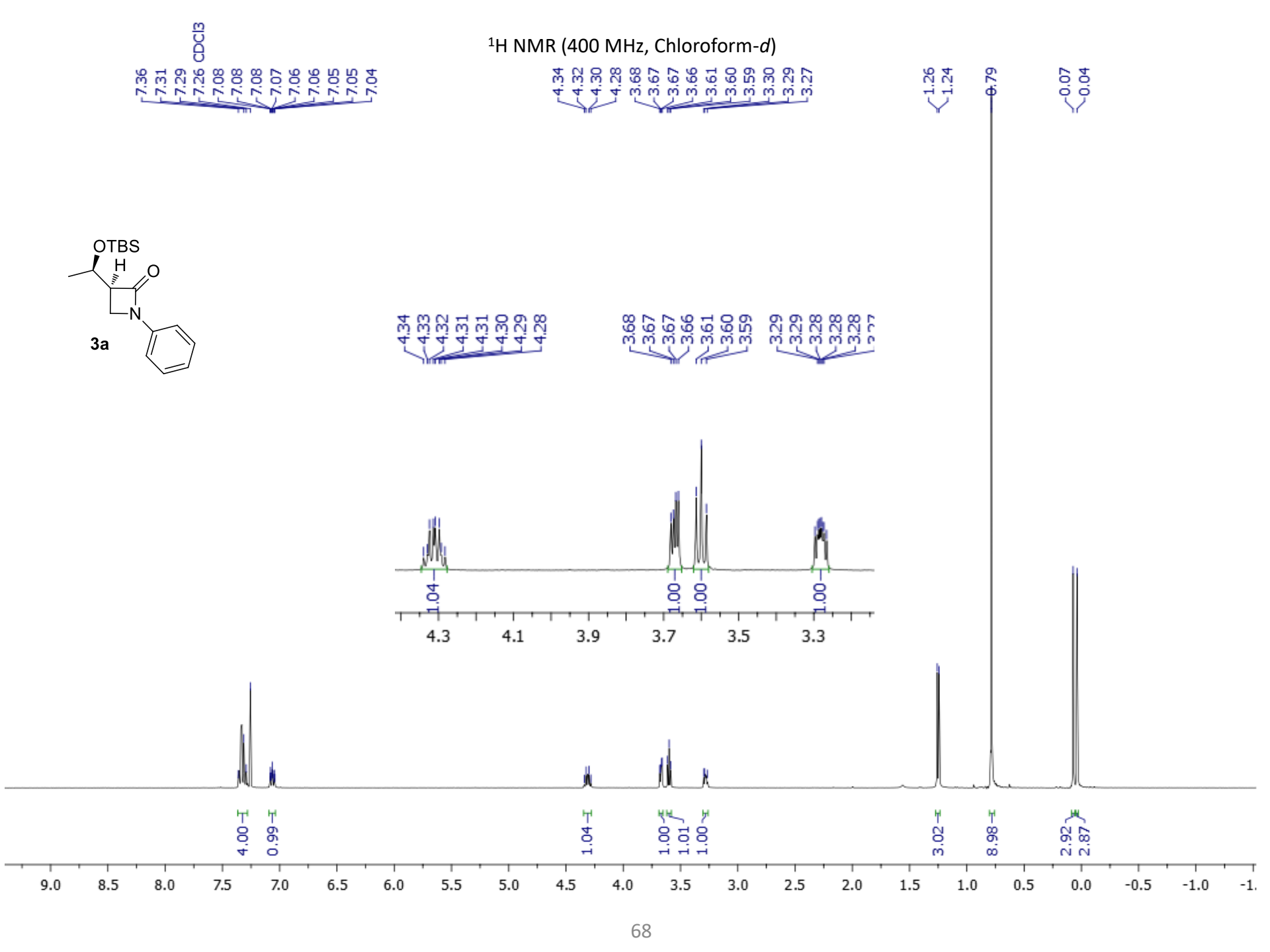


2l

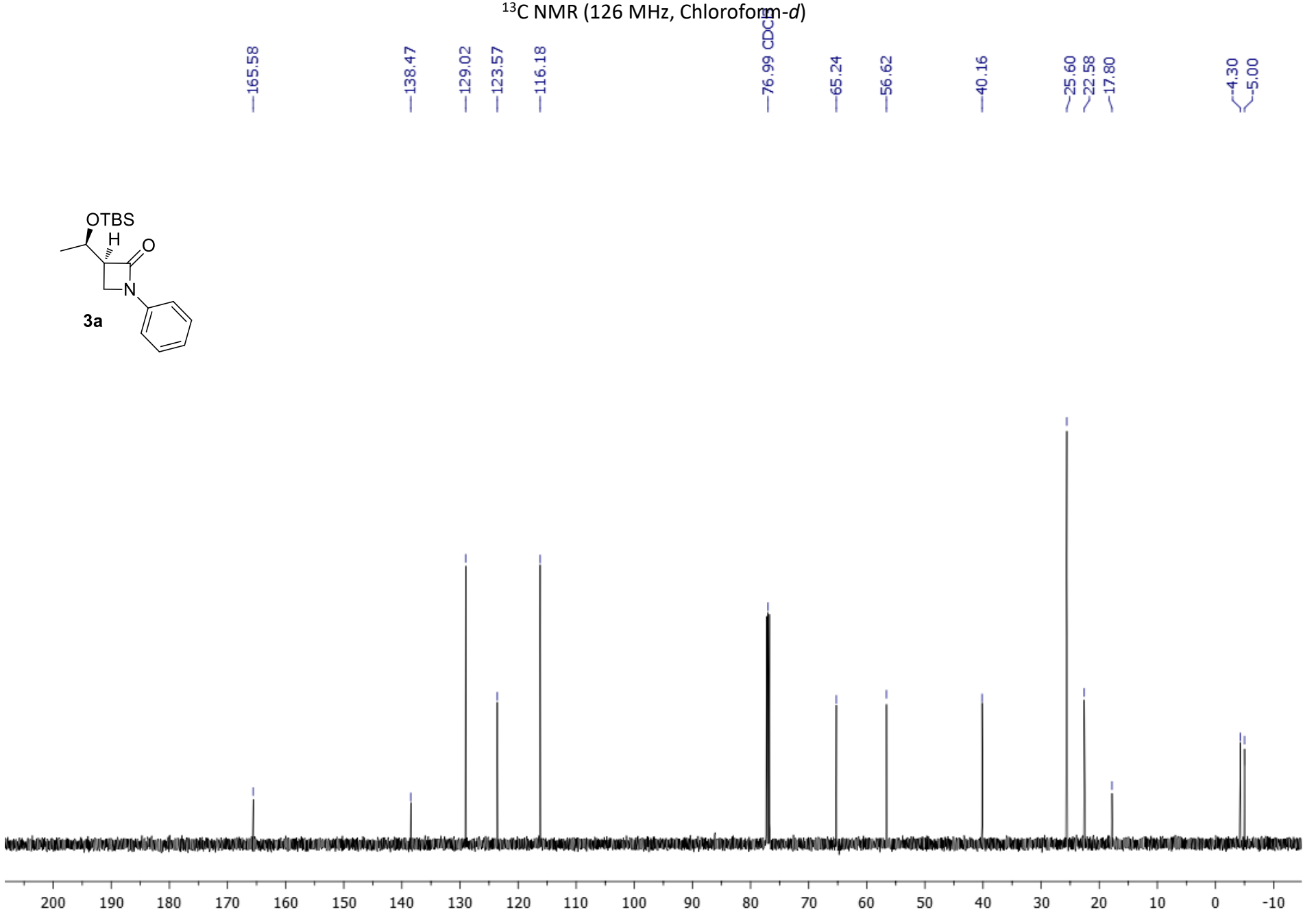
^{13}C NMR (101 MHz, Chloroform-*d*) δ



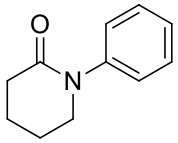
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (126 MHz, Chloroform-*d*)

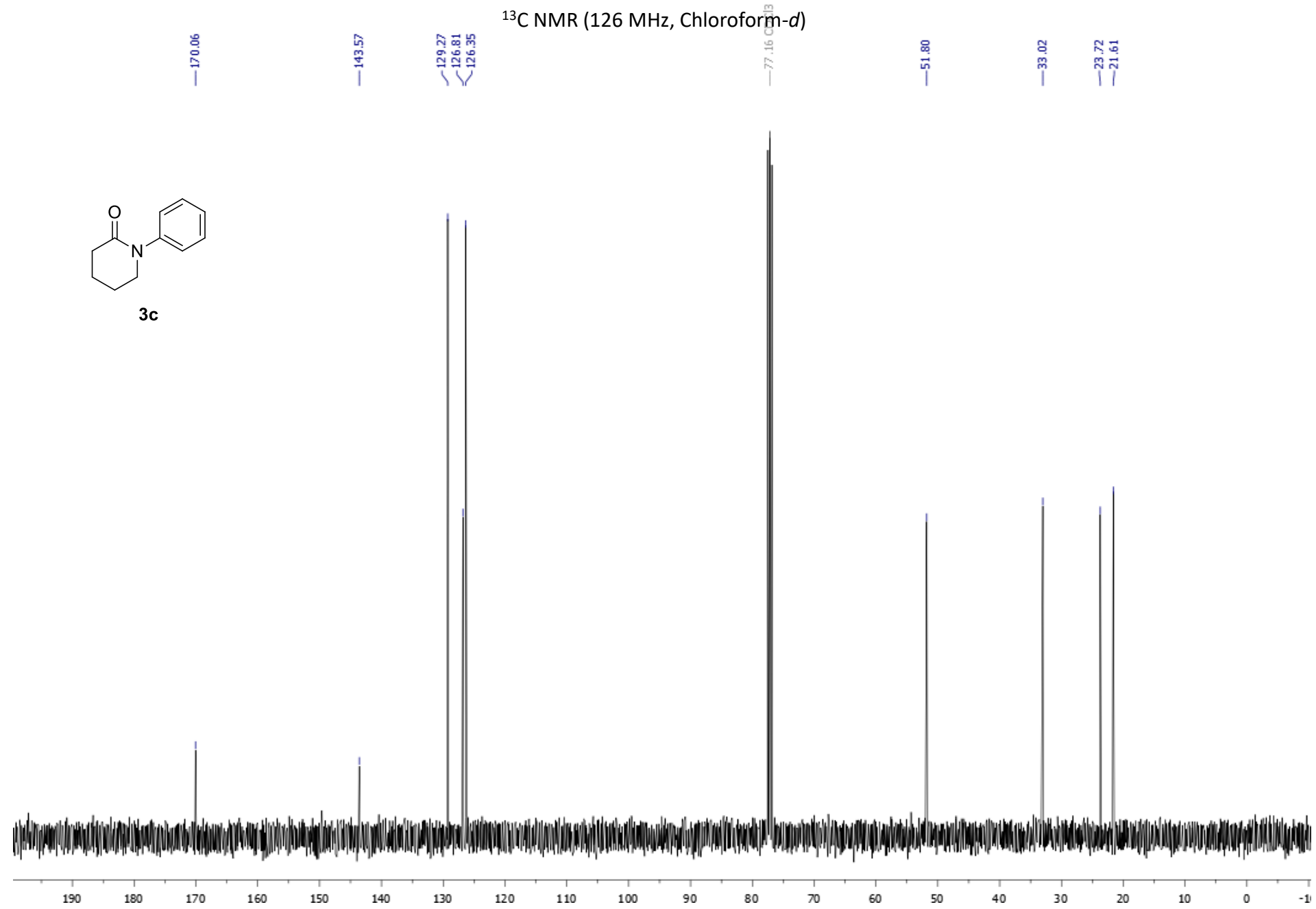


^{1}H NMR (400 MHz, Chloroform-*d*)

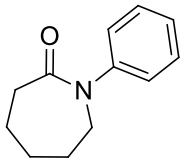


3c

^{13}C NMR (126 MHz, Chloroform-*d*)

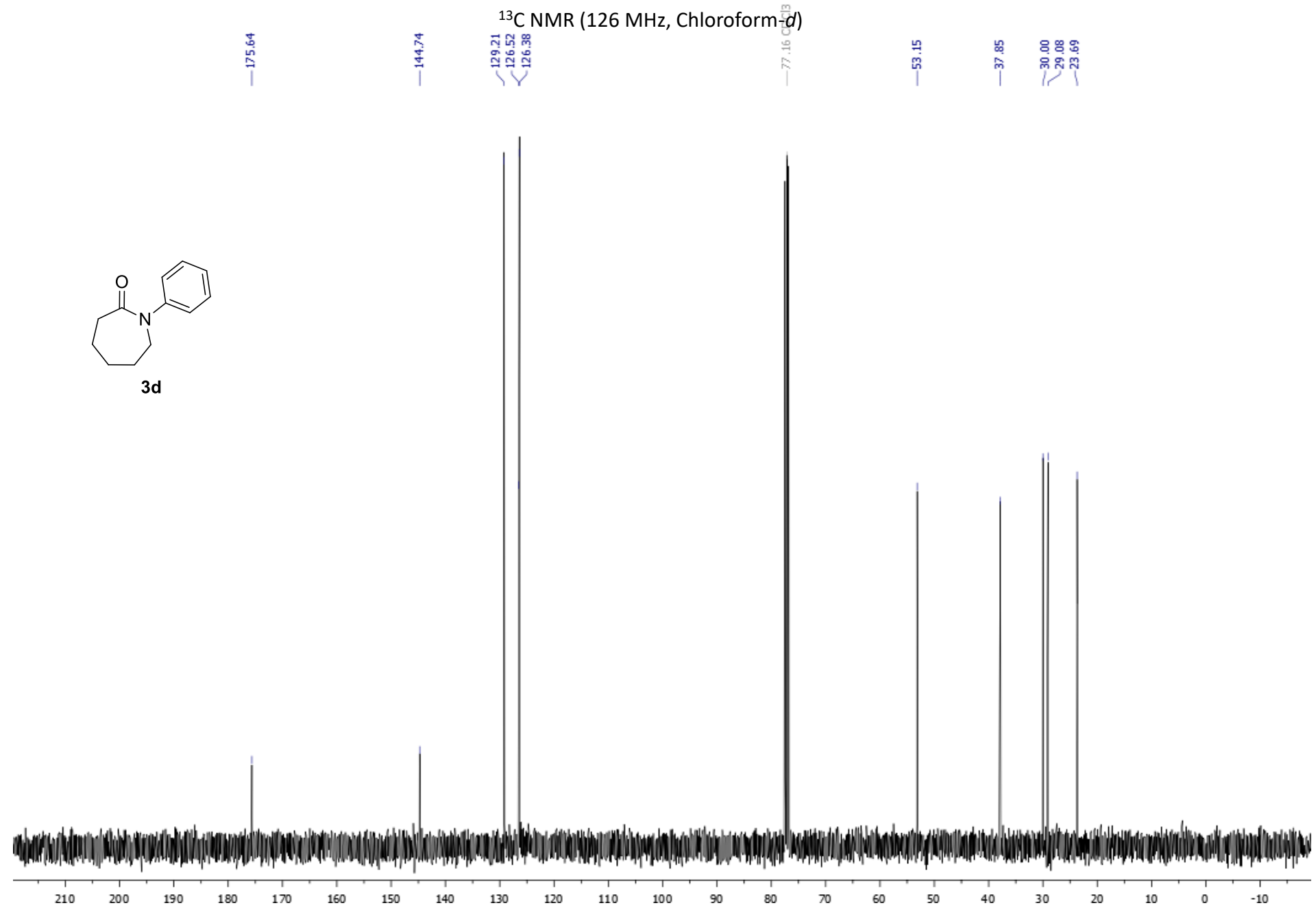


^{1}H NMR (400 MHz, Chloroform-*d*)

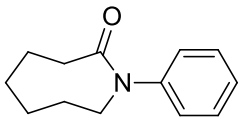


3d

^{13}C NMR (126 MHz, Chloroform-*d*)

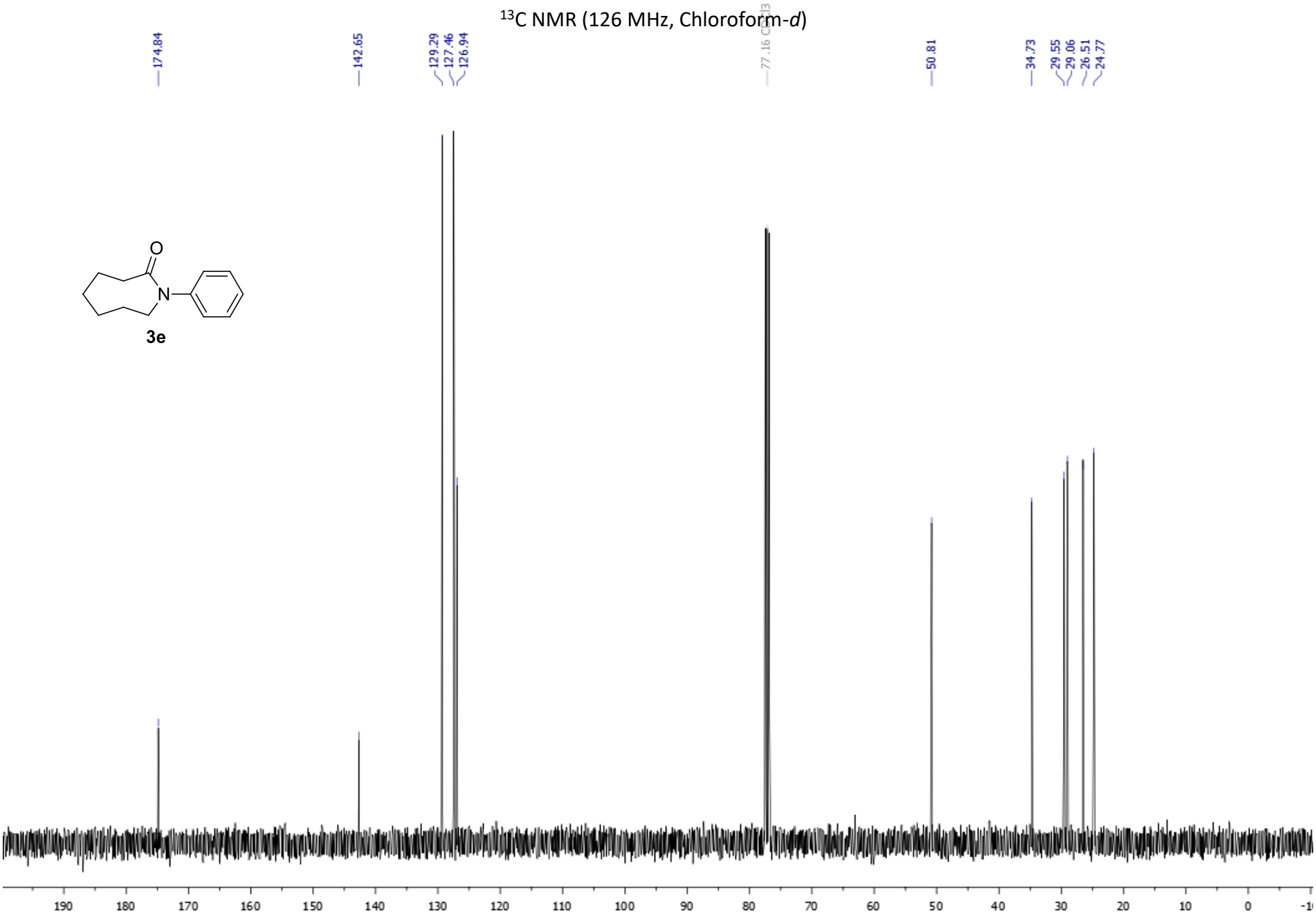


^{1}H NMR (400 MHz, Chloroform-*d*)

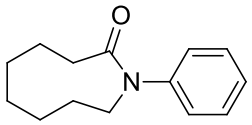


3e

^{13}C NMR (126 MHz, Chloroform-*d*)

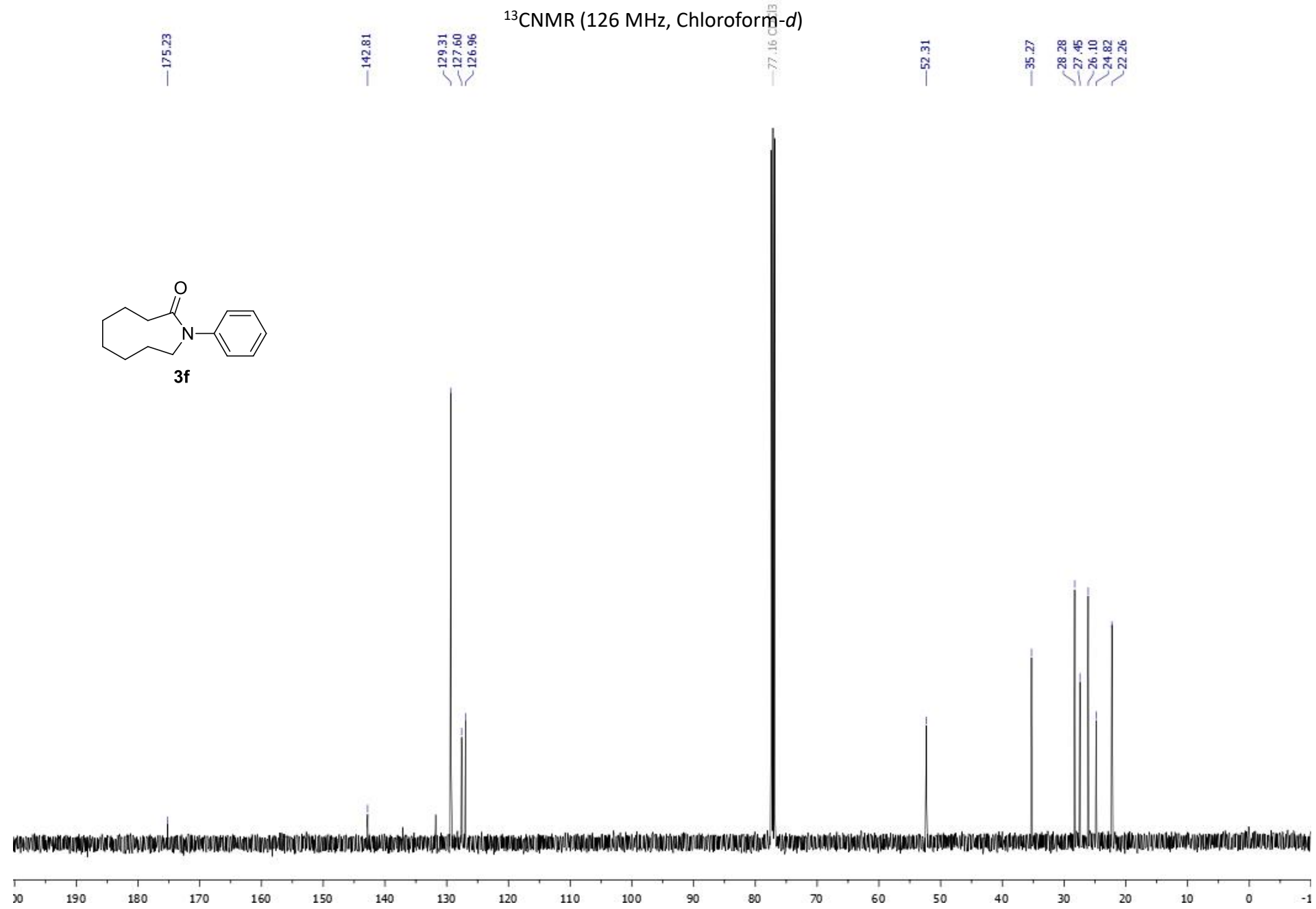


^{1}H NMR (400 MHz, Chloroform-*d*)

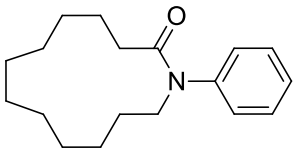


3f

^{13}CNMR (126 MHz, Chloroform-*d*)

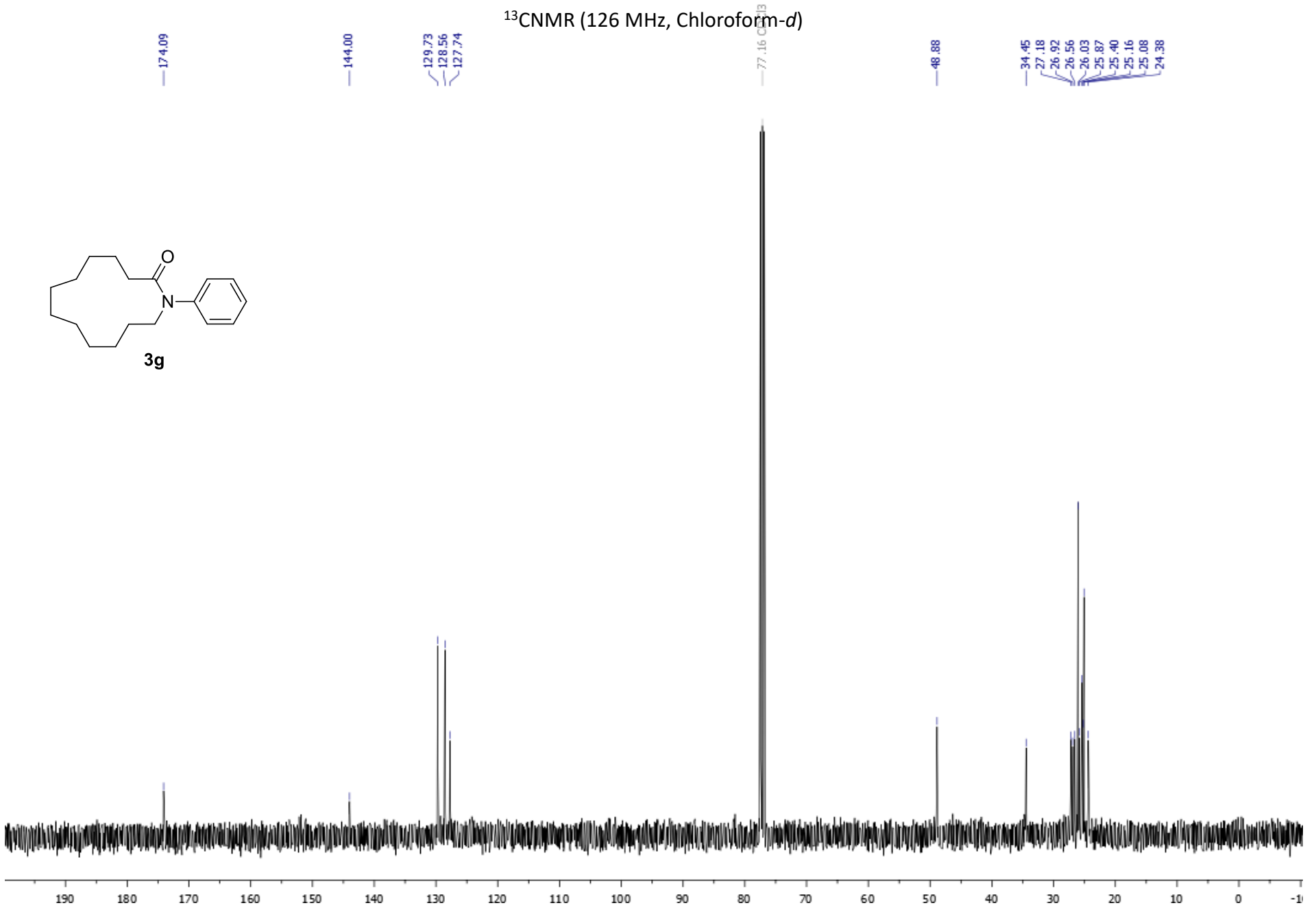


^{1}H NMR (400 MHz, Chloroform-*d*)

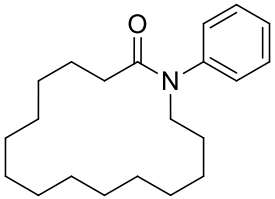


3g

^{13}CNMR (126 MHz, Chloroform-*d*)

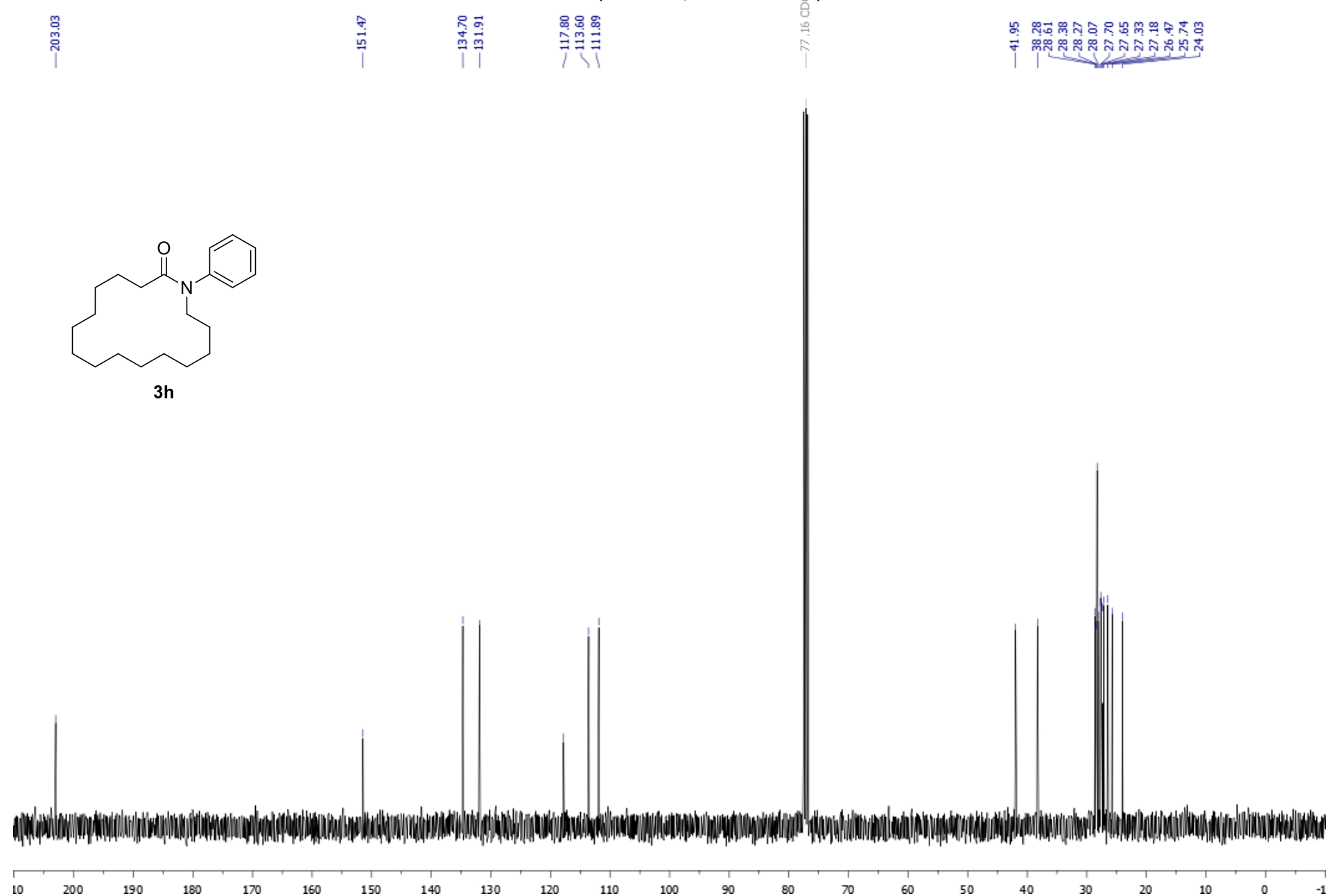


^{1}H NMR (400 MHz, Chloroform-*d*)

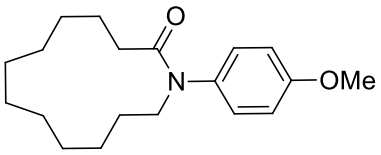


3h

^{13}C NMR (126 MHz, Chloroform-*d*)

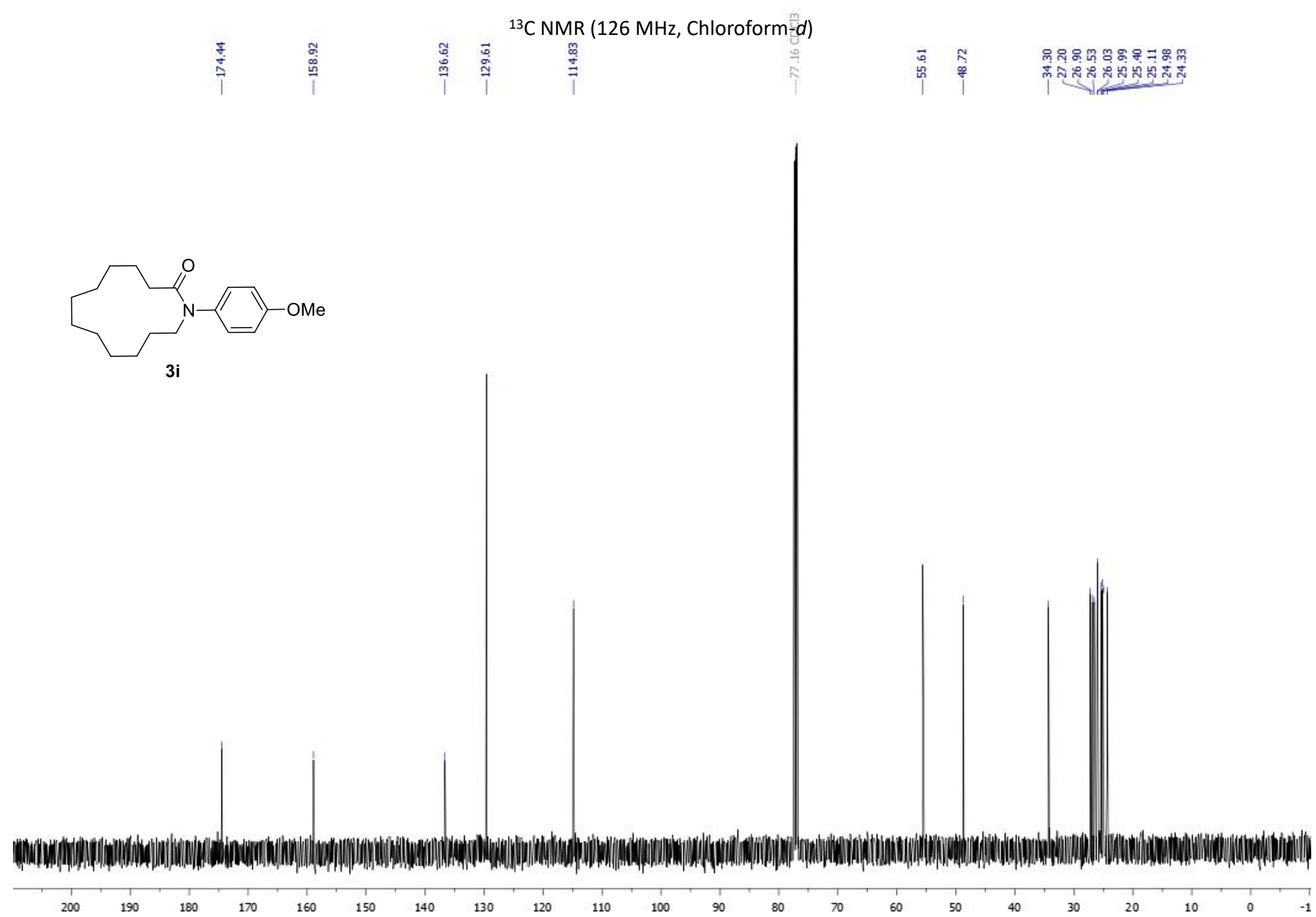


^{1}H NMR (400 MHz, Chloroform-*d*)

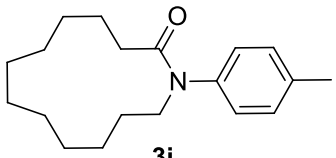


3i

^{13}C NMR (126 MHz, Chloroform-*d*)

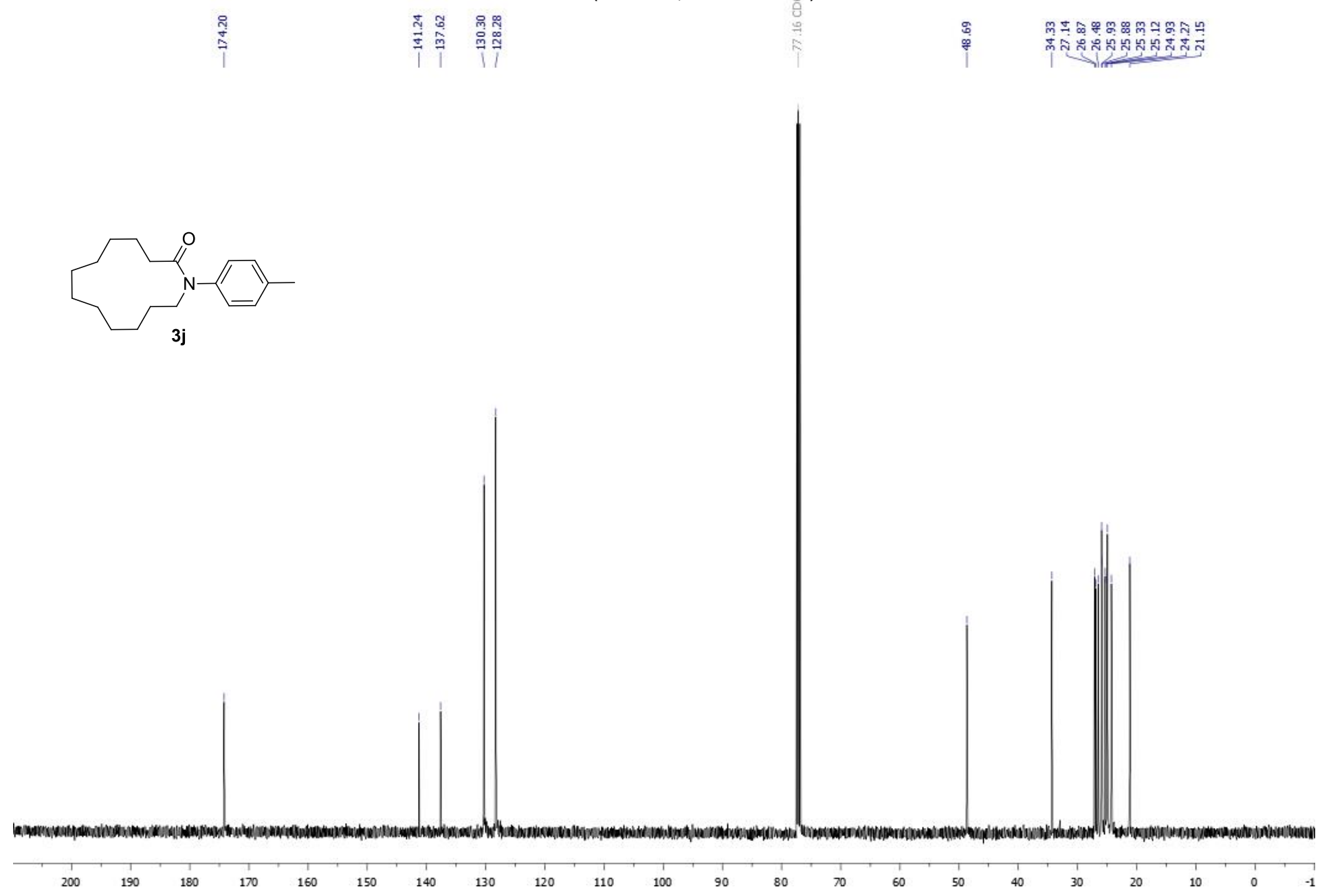


^{1}H NMR (400 MHz, Chloroform-*d*)

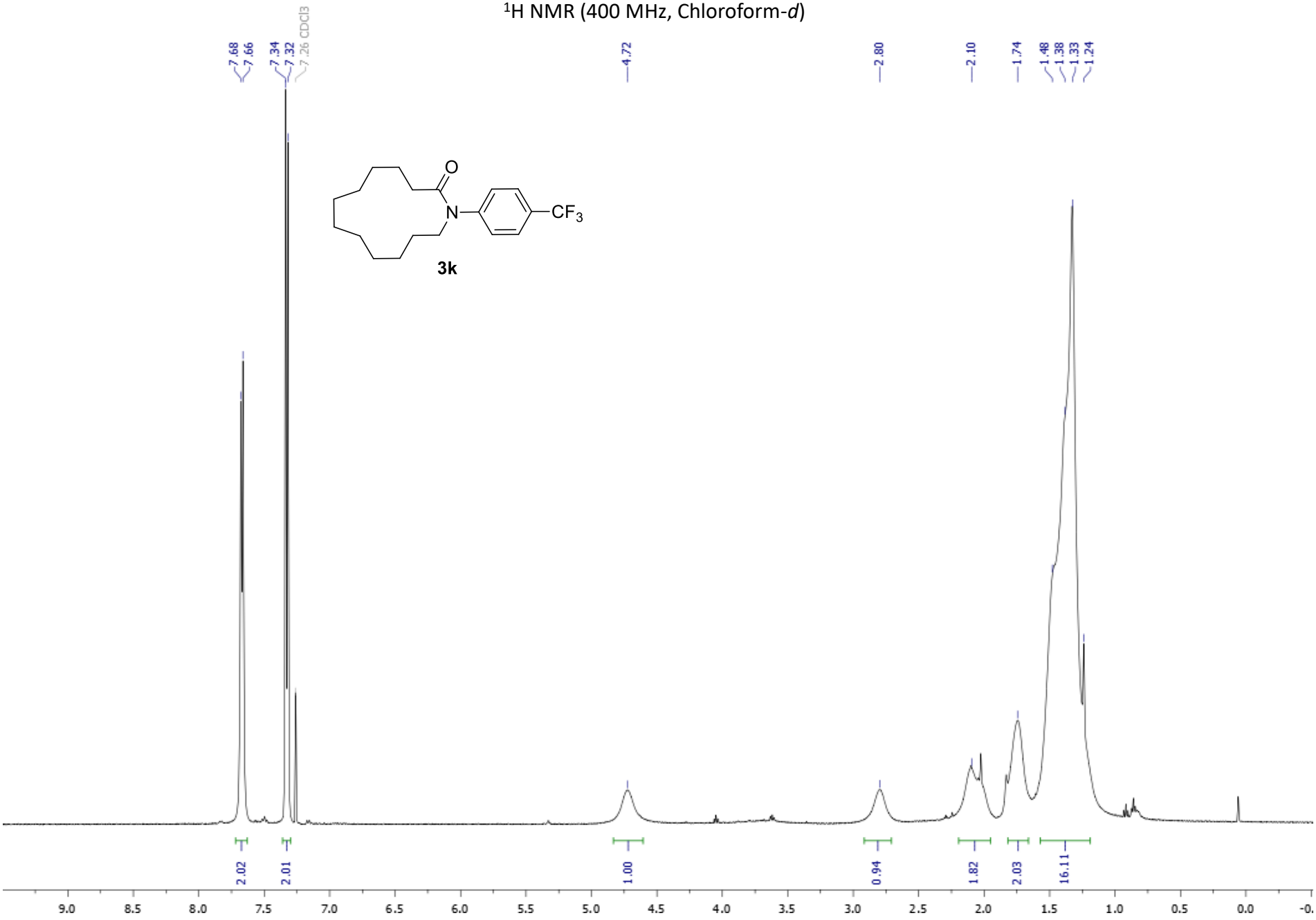


3j

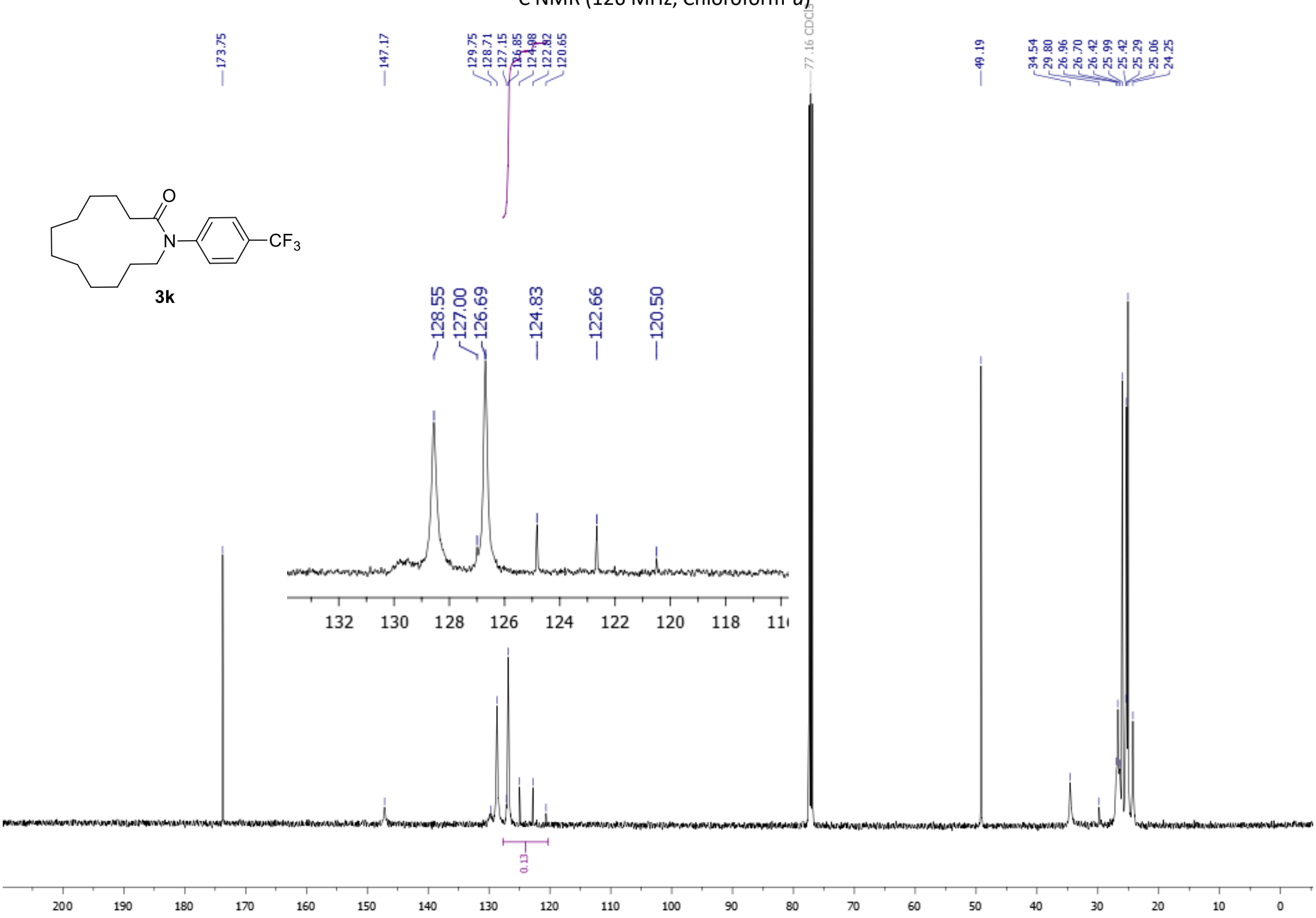
^{13}C NMR (126 MHz, Chloroform-*d*)



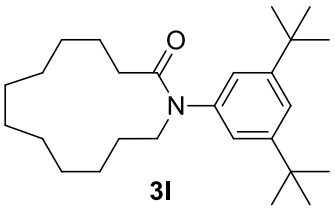
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (126 MHz, Chloroform-*d*)

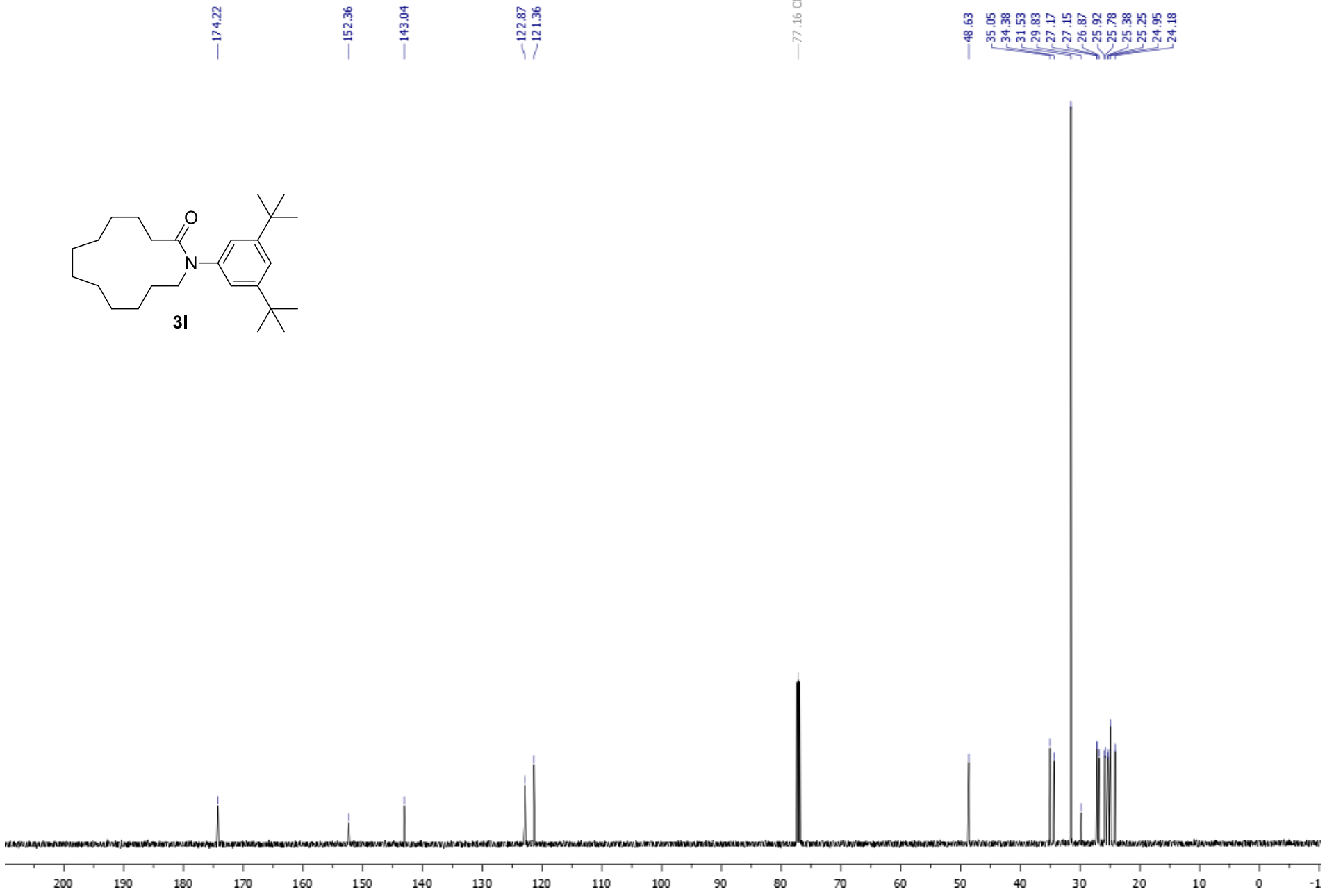


^{1}H NMR (500 MHz, Chloroform-*d*)

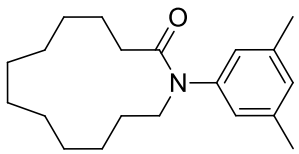


3l

^{13}C NMR (126 MHz, Chloroform-*d*)

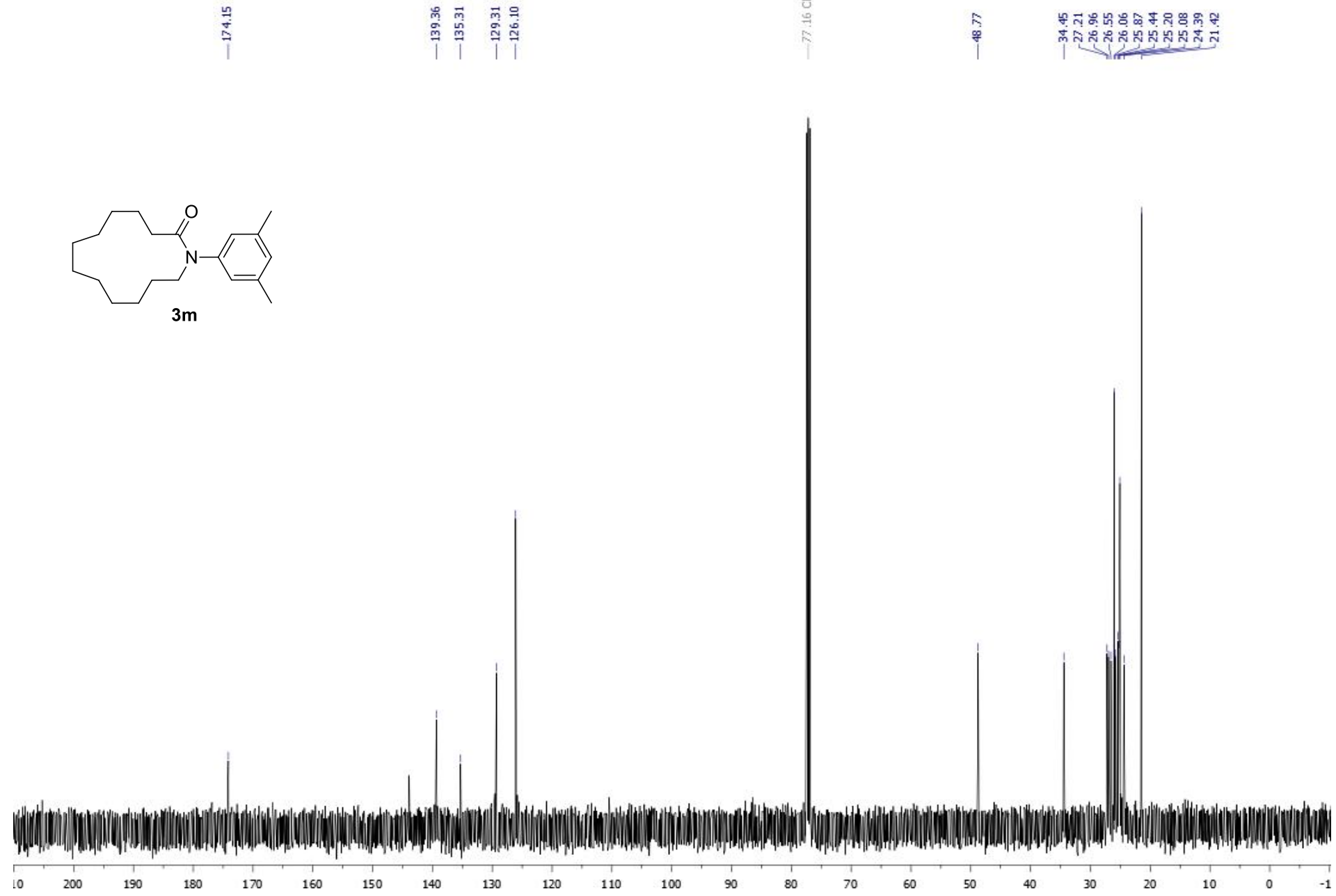


^{1}H NMR (500 MHz, Chloroform-*d*)

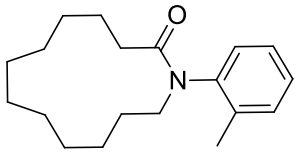


3m

^{13}C NMR (126 MHz, Chloroform-*d*)

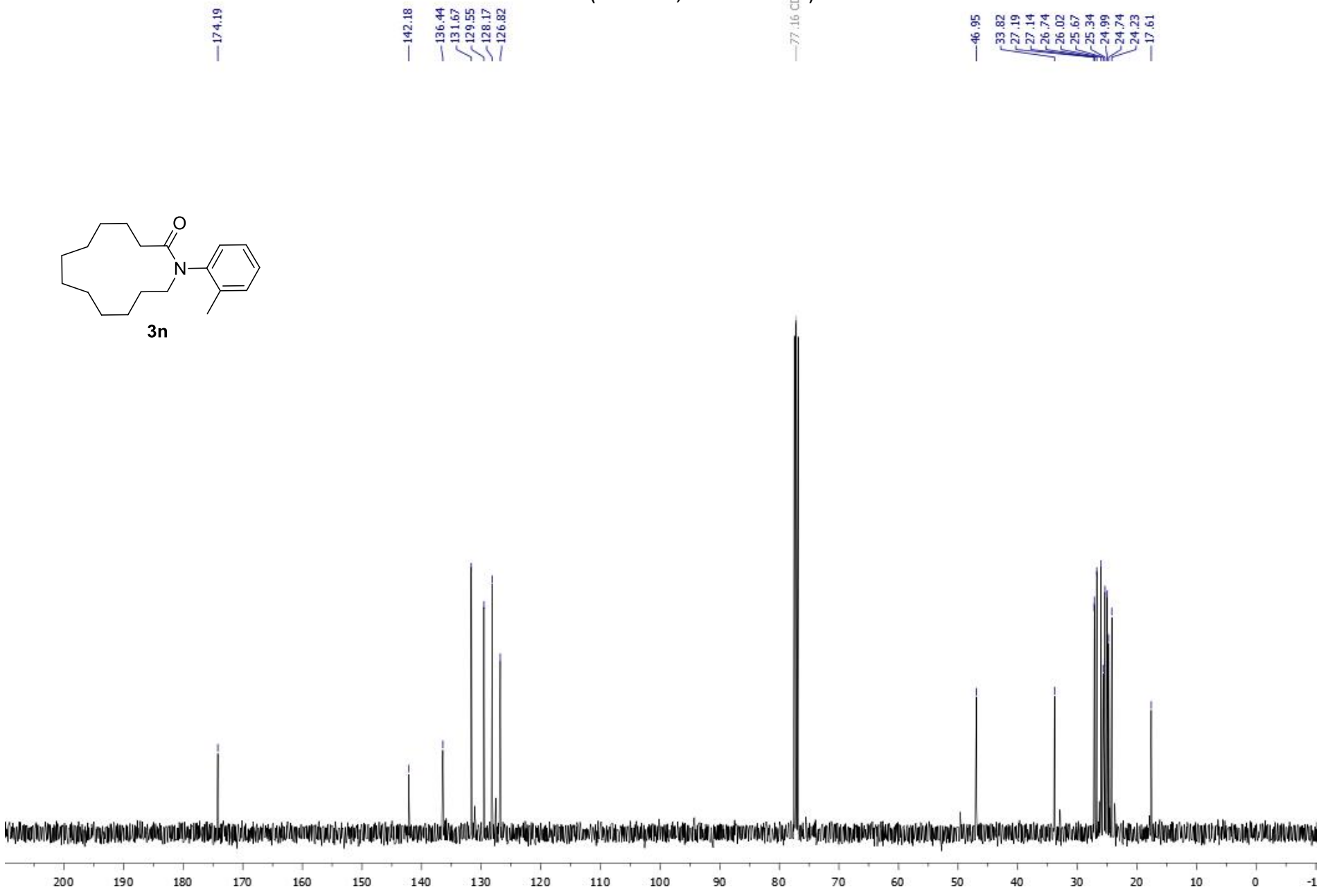


^{1}H NMR (400 MHz, Chloroform-*d*)

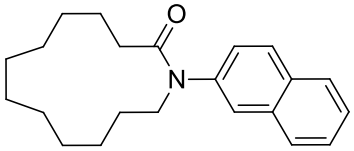


3n

^{13}C NMR (101 MHz, Chloroform-*d*)

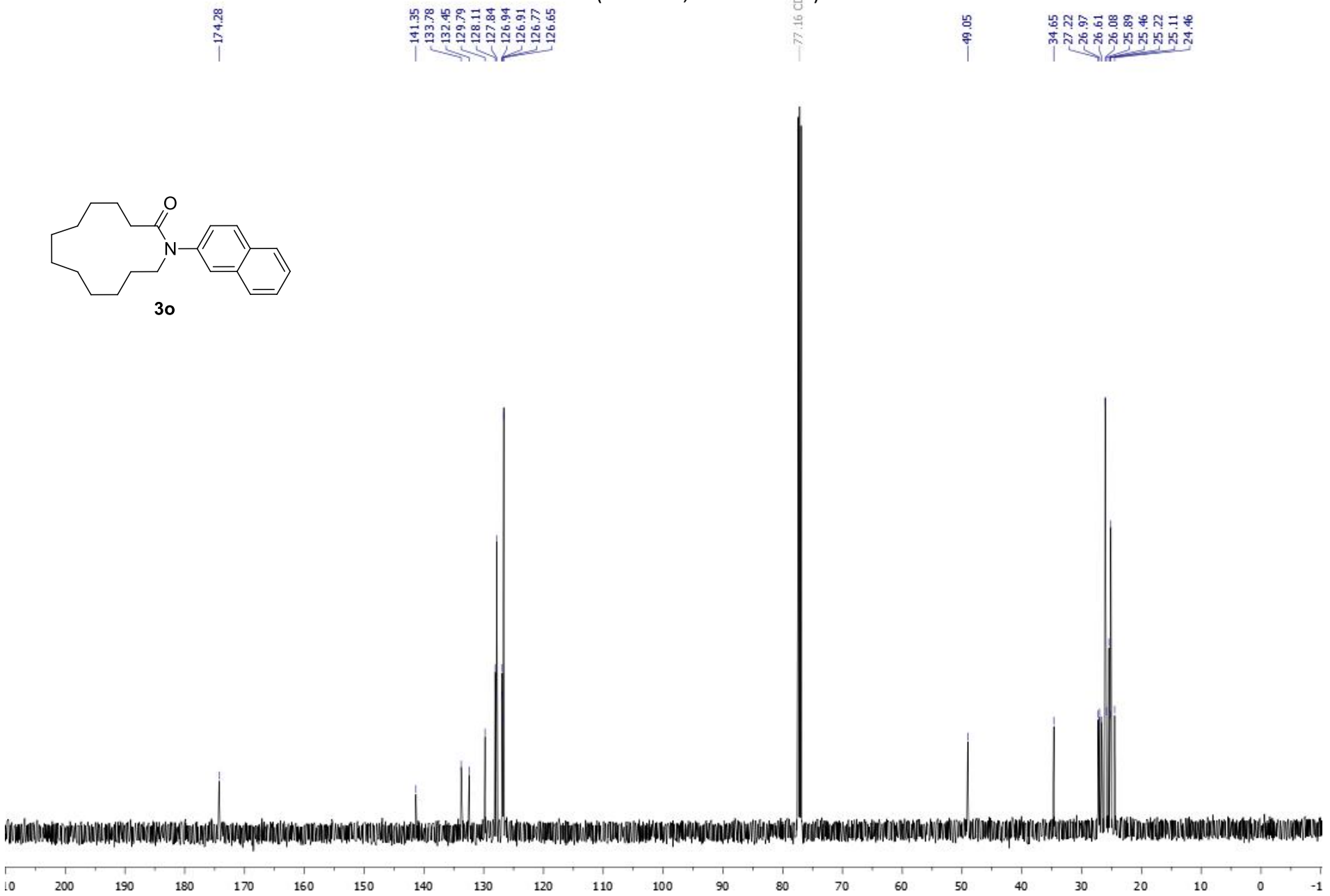


^{1}H NMR (400 MHz, chloroform-*d*)

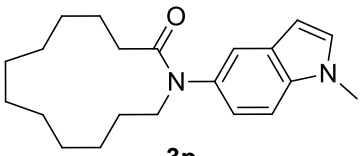


3o

^{13}C NMR (126 MHz, chloroform-*d*)

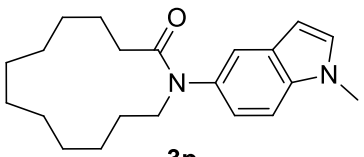


^{1}H NMR (500 MHz, Chloroform-*d*)

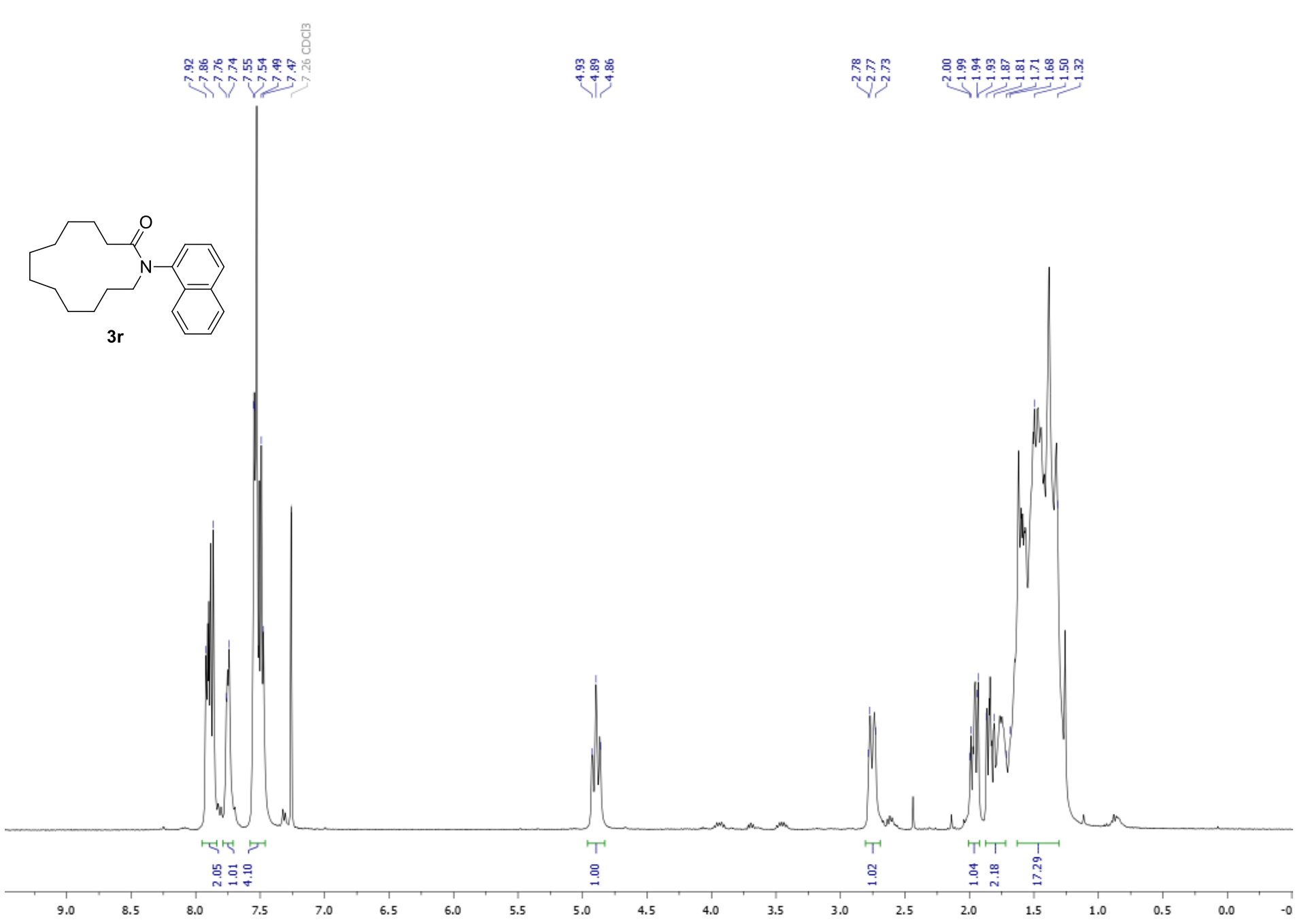


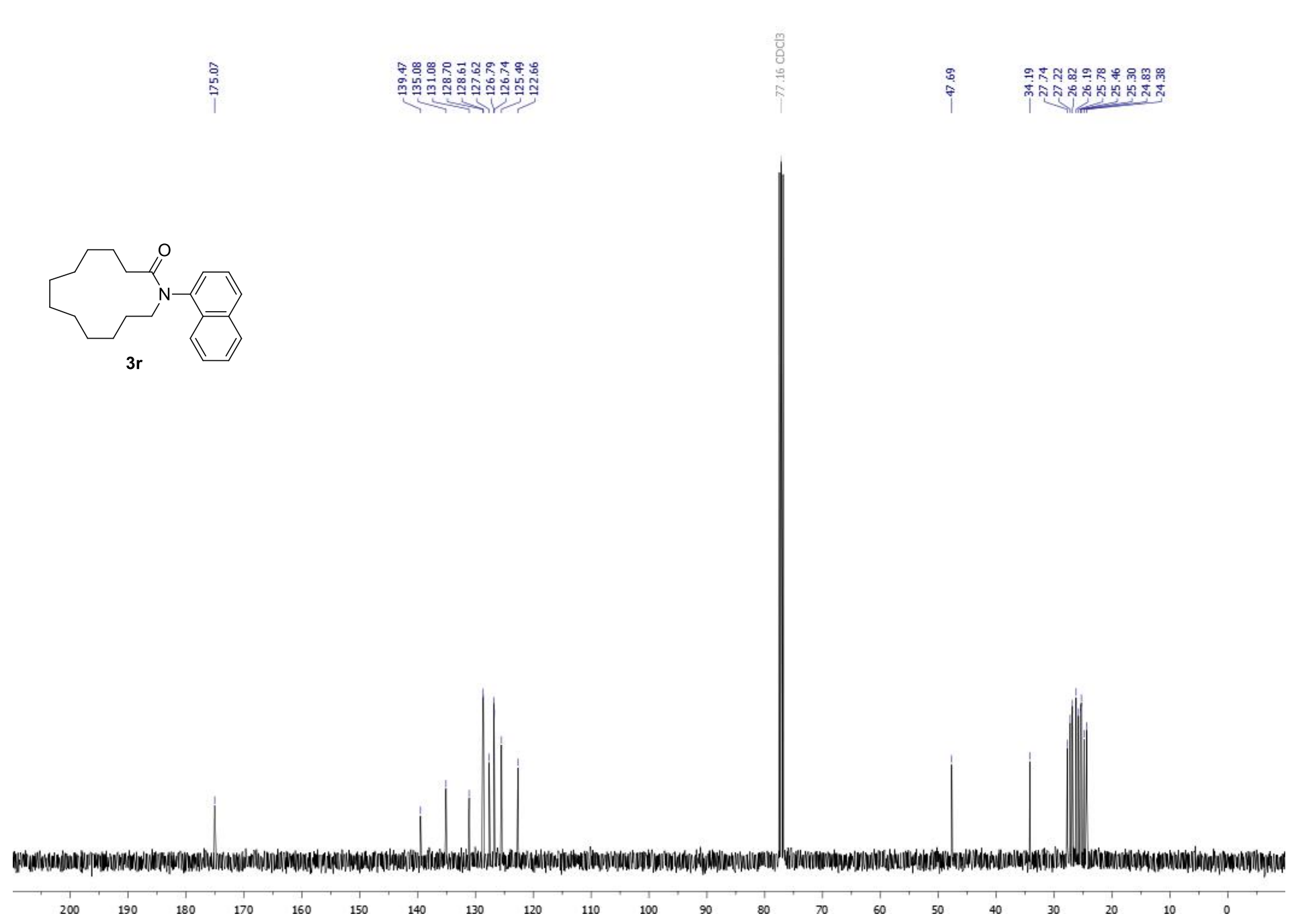
3p

^{13}C NMR (126 MHz, Chloroform-*d*)

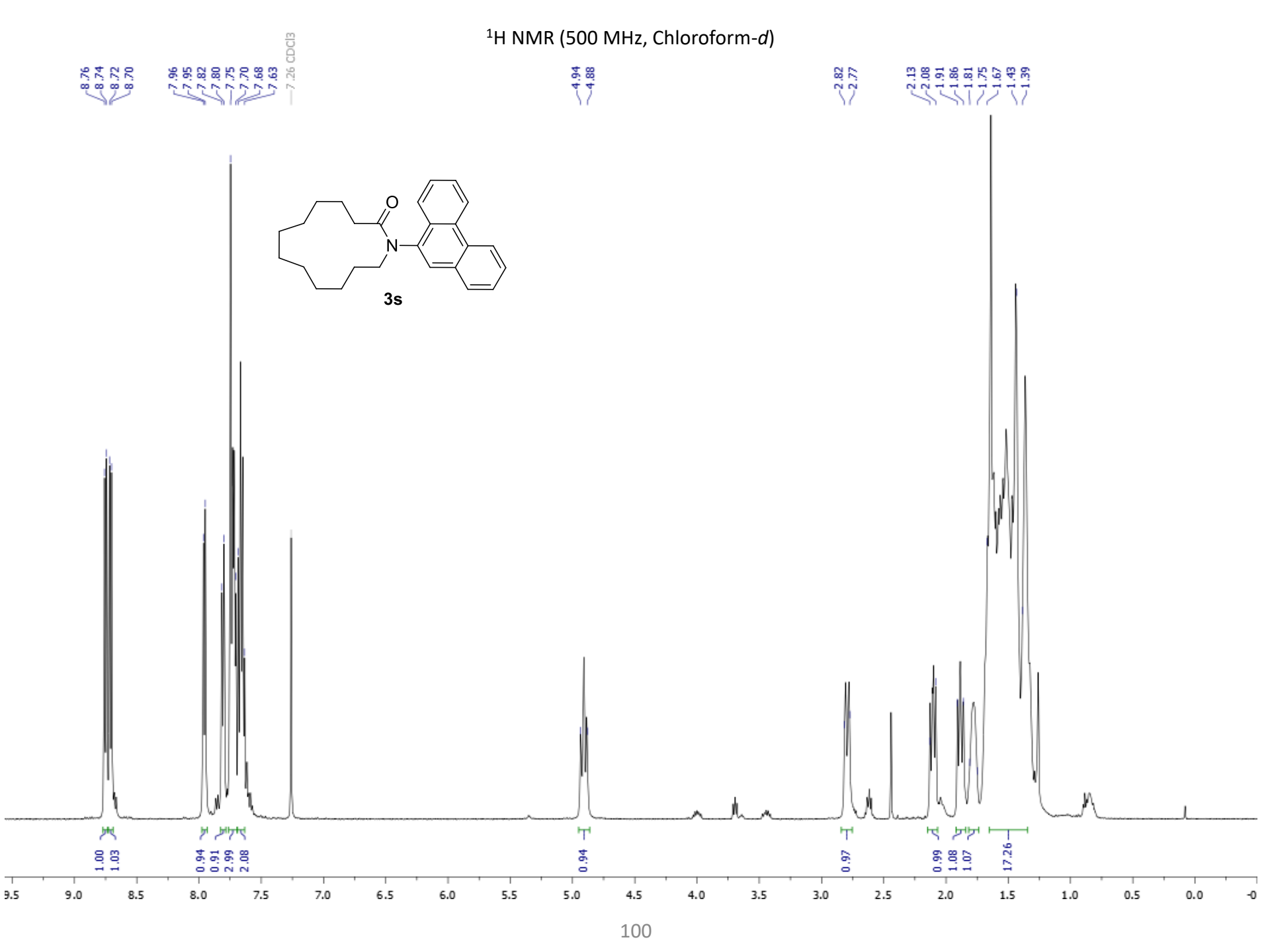


3p

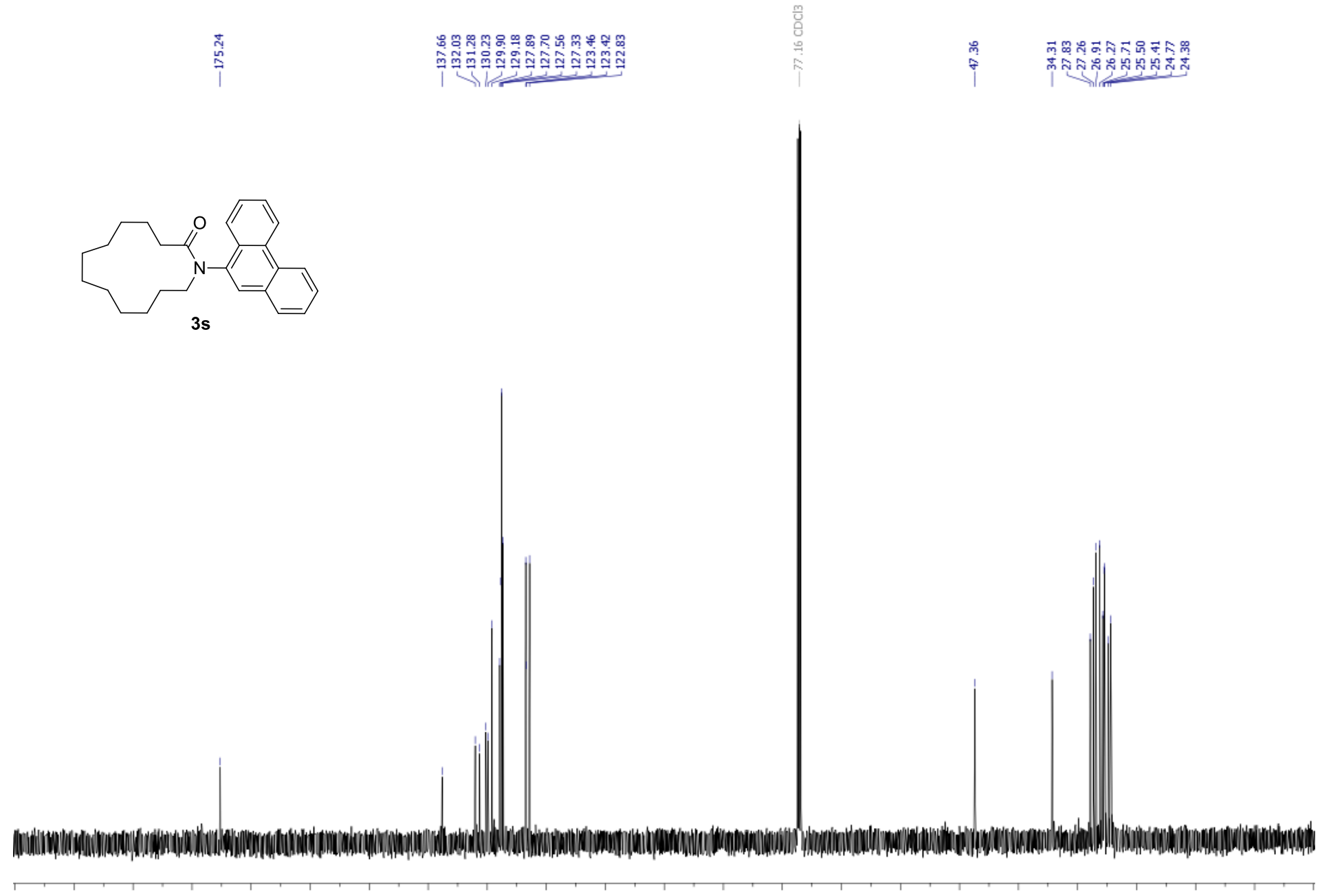

7.92
7.86
7.76
7.74
7.55
7.54
7.49
7.47
7.26 CDCl3
4.93
4.89
4.86
2.78
2.77
2.73
2.00
1.99
1.94
1.93
1.87
1.81
1.71
1.68
1.50
1.32
O
N
3r
2.05
1.01
4.10
1.00
1.02
1.04
2.18
17.29
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0


175.07
139.47
135.08
131.08
128.70
128.61
127.62
126.79
126.74
125.49
122.66
77.16 CDCl3
47.69
34.19
27.74
27.22
26.82
26.19
25.78
25.46
25.30
24.83
24.38
O
N
3r
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

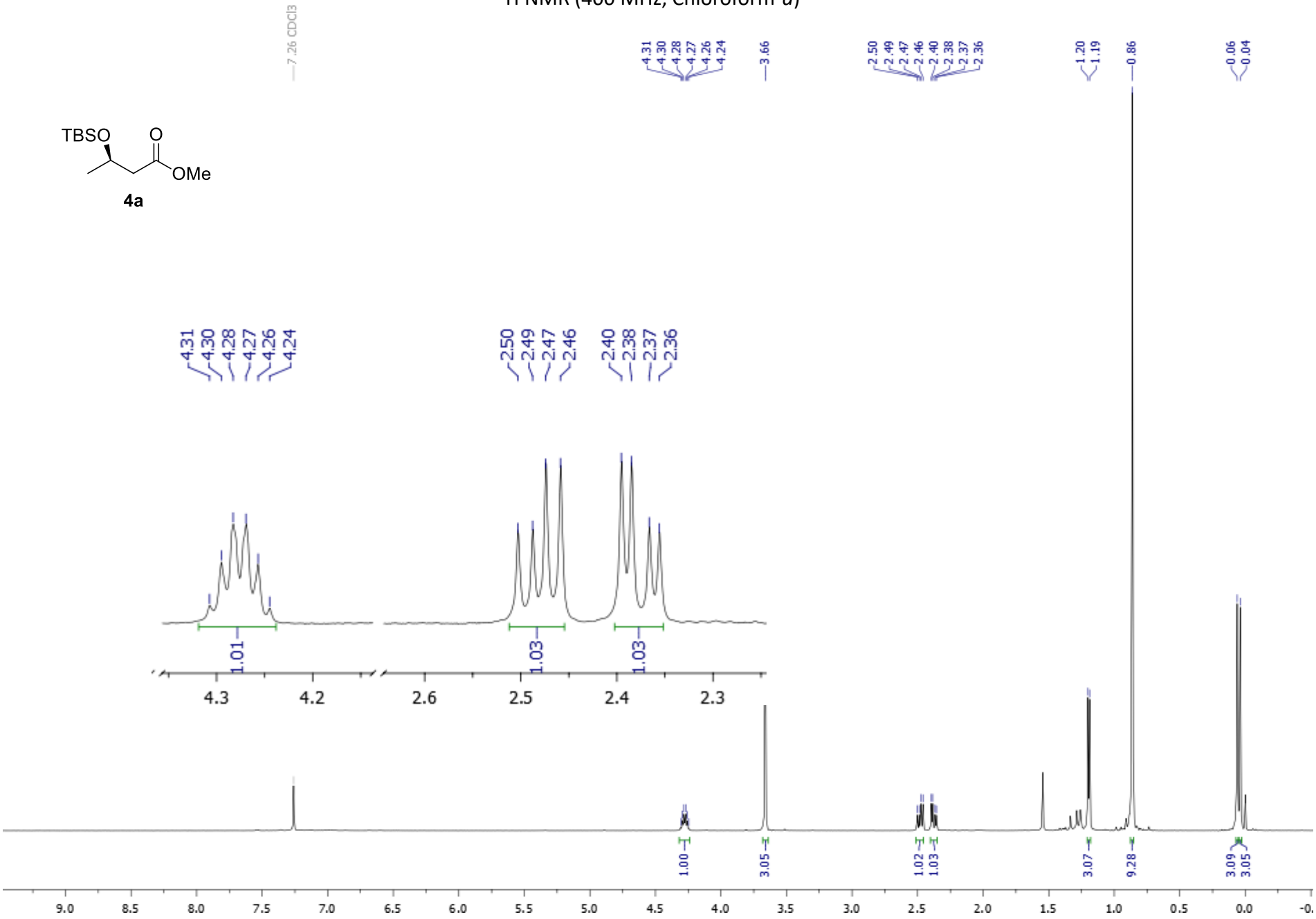
^{1}H NMR (500 MHz, Chloroform-*d*)



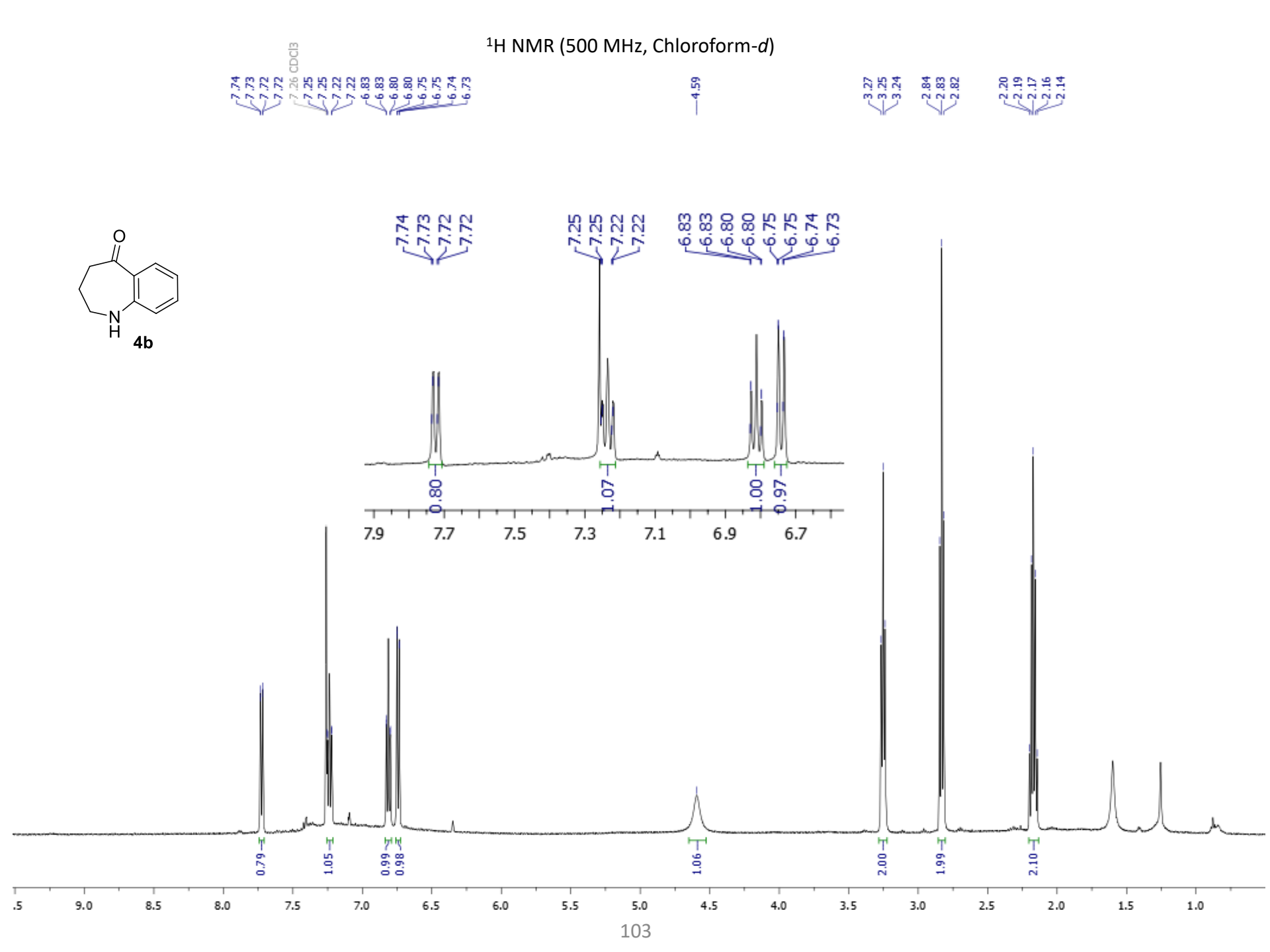
^{13}C NMR (126 MHz, Chloroform-*d*)



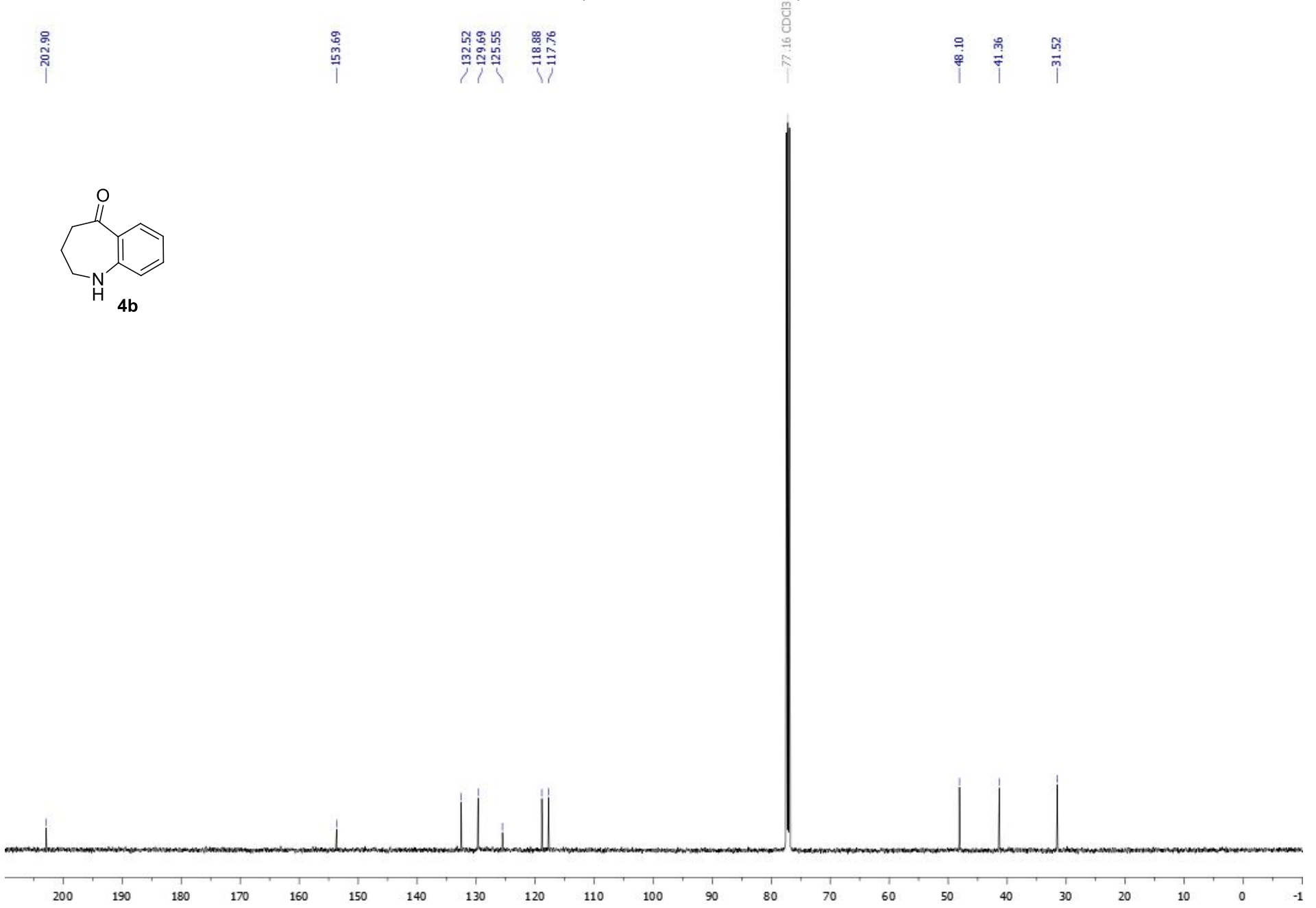
^{1}H NMR (400 MHz, Chloroform-*d*)



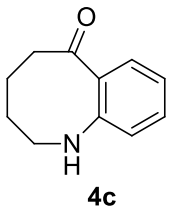
^{1}H NMR (500 MHz, Chloroform-*d*)



^{13}C NMR (126 MHz, Chloroform-*d*)

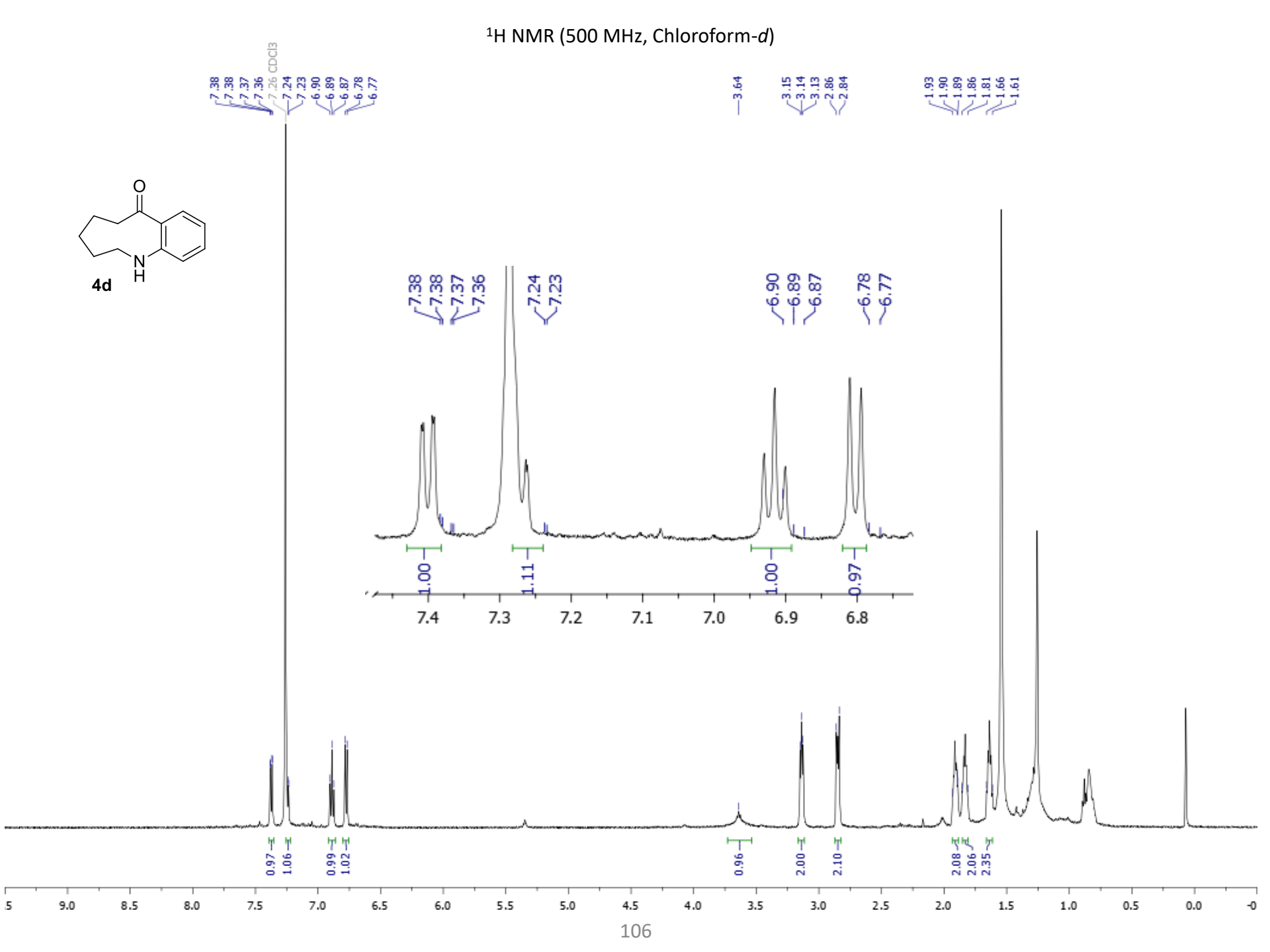


^{1}H NMR (400 MHz, Chloroform-*d*)

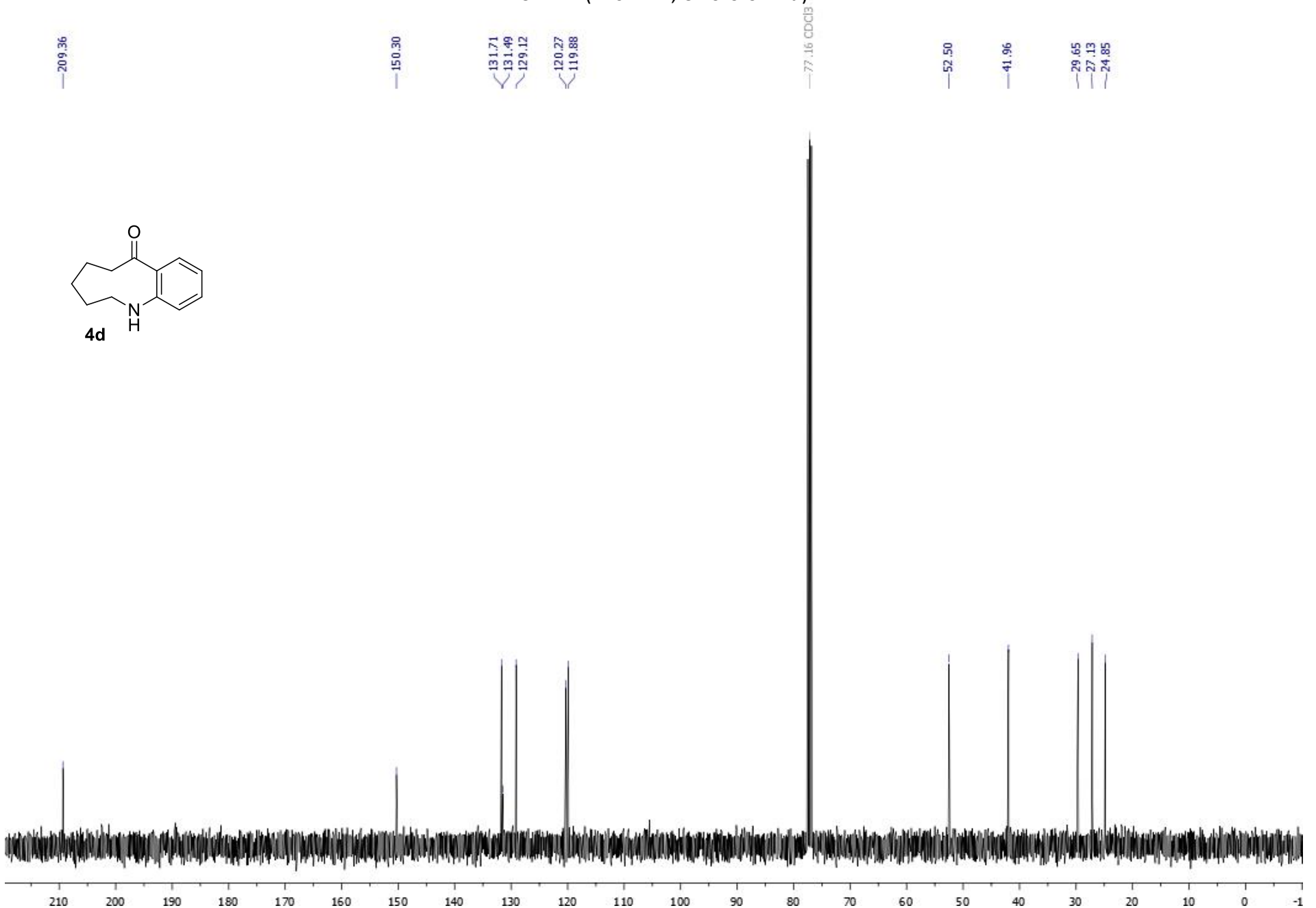


4c

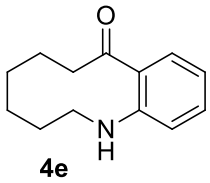
^{1}H NMR (500 MHz, Chloroform-*d*)



^{13}C NMR (126 MHz, Chloroform-*d*)

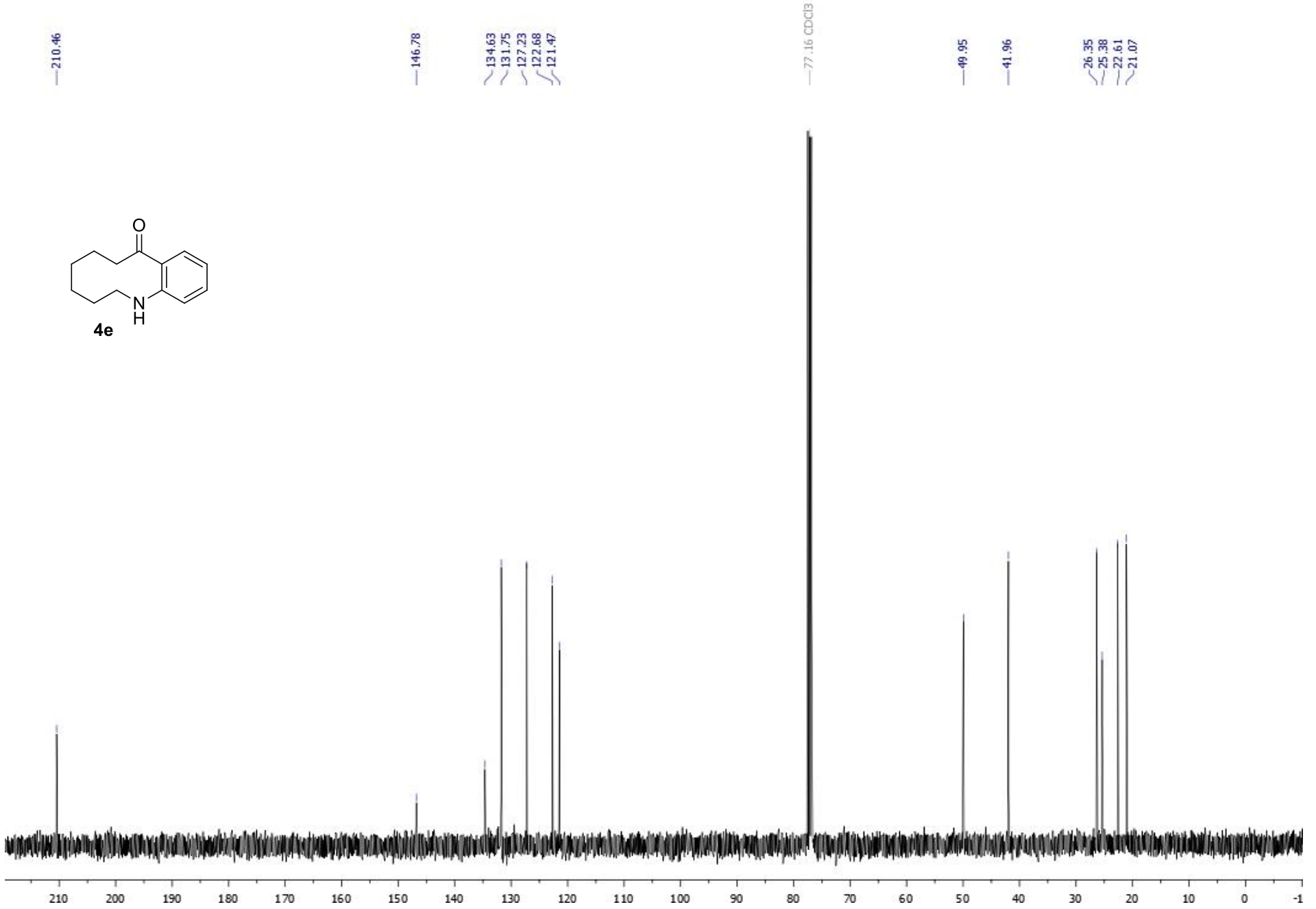


^{1}H NMR (500 MHz, Chloroform-*d*)

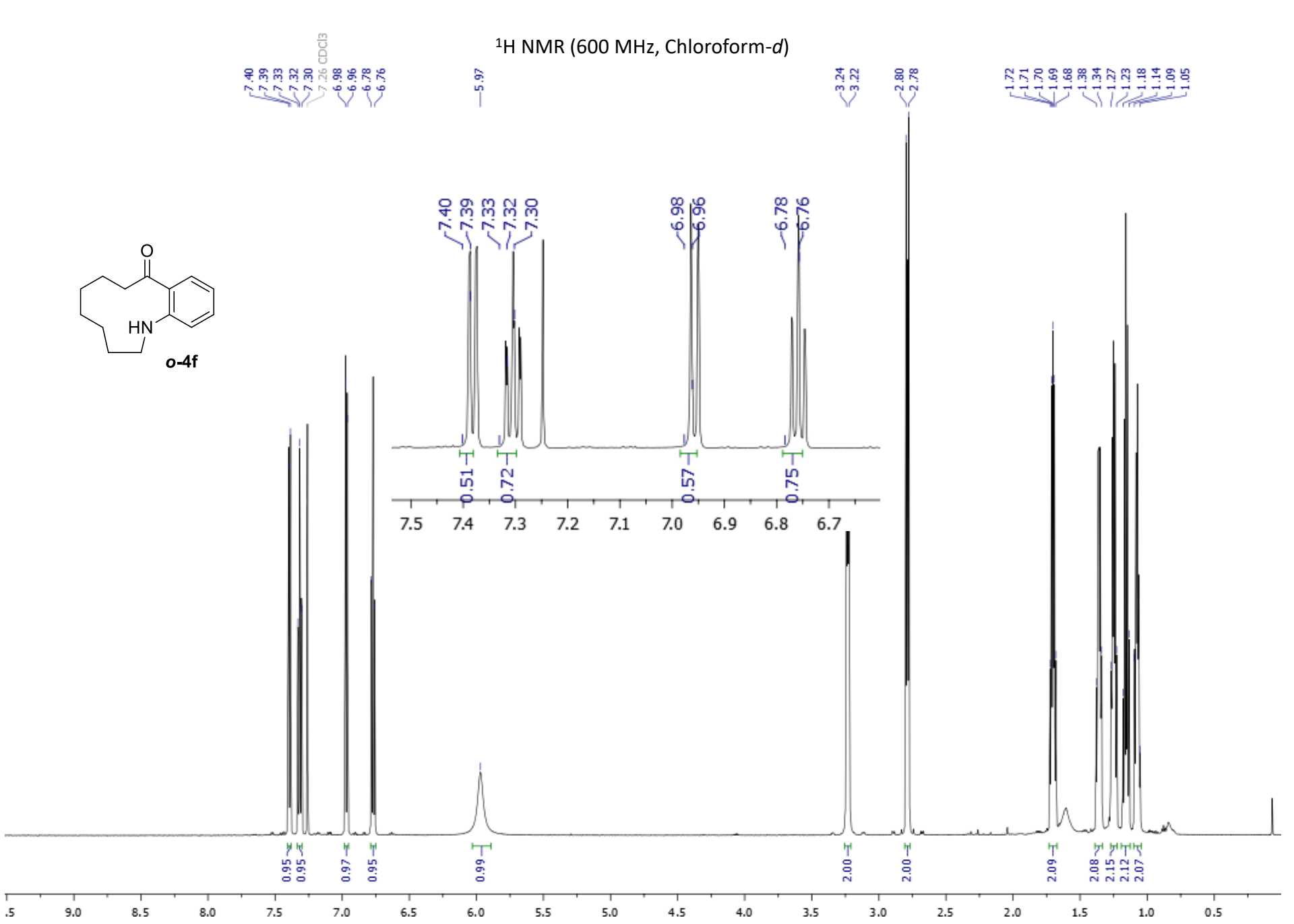


4e

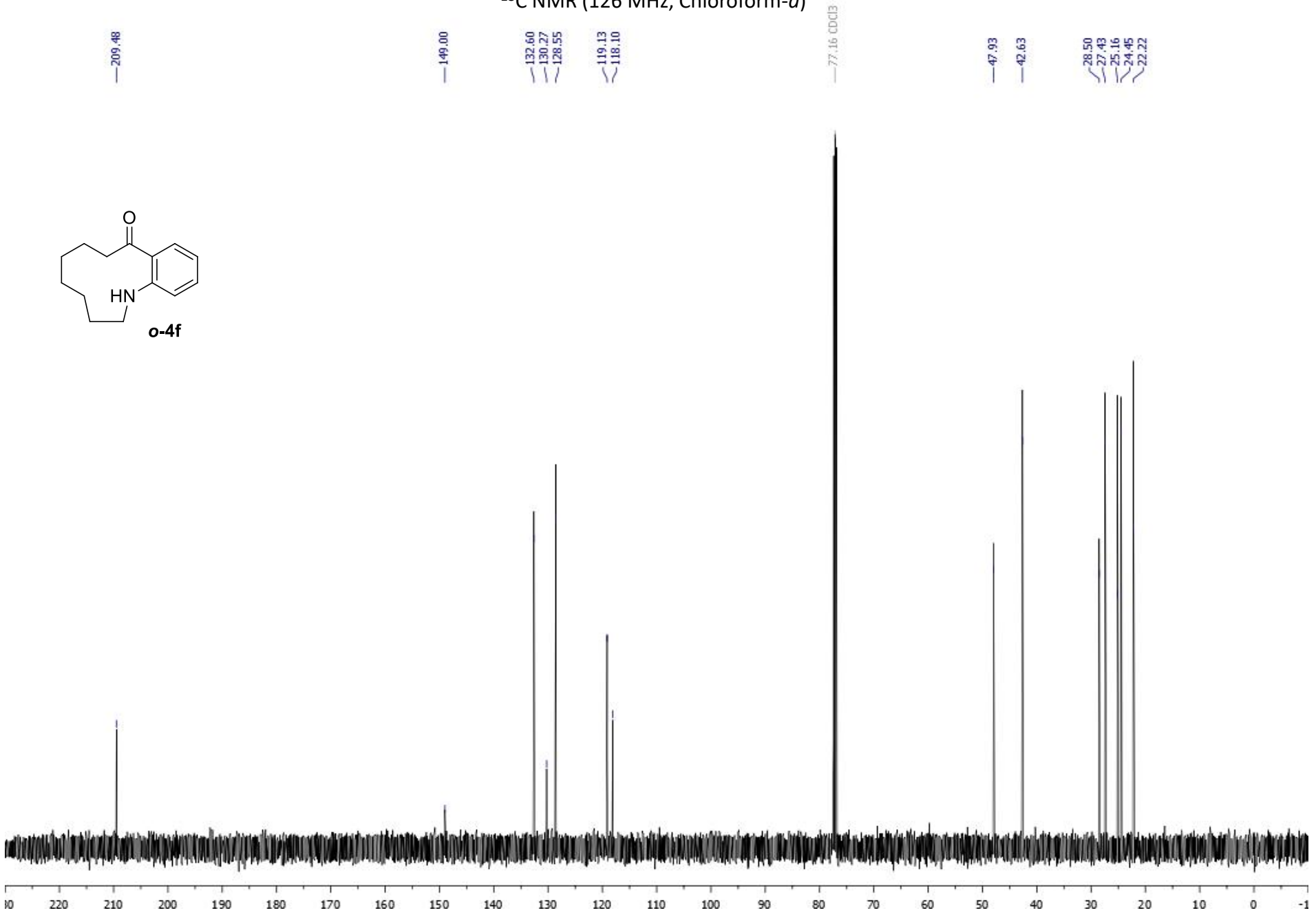
^{13}C NMR (101 MHz, Chloroform-*d*)



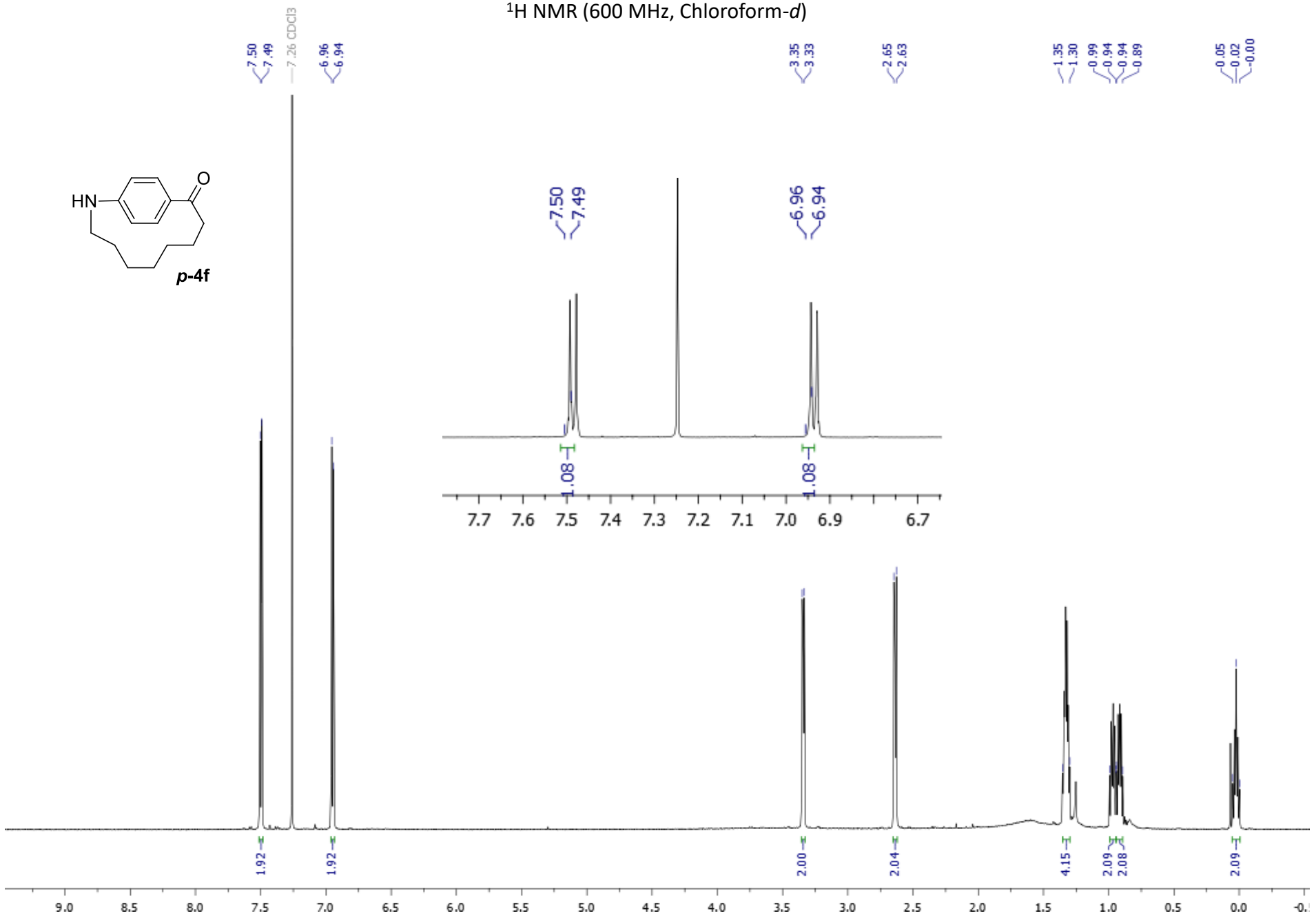
^{1}H NMR (600 MHz, Chloroform-*d*)



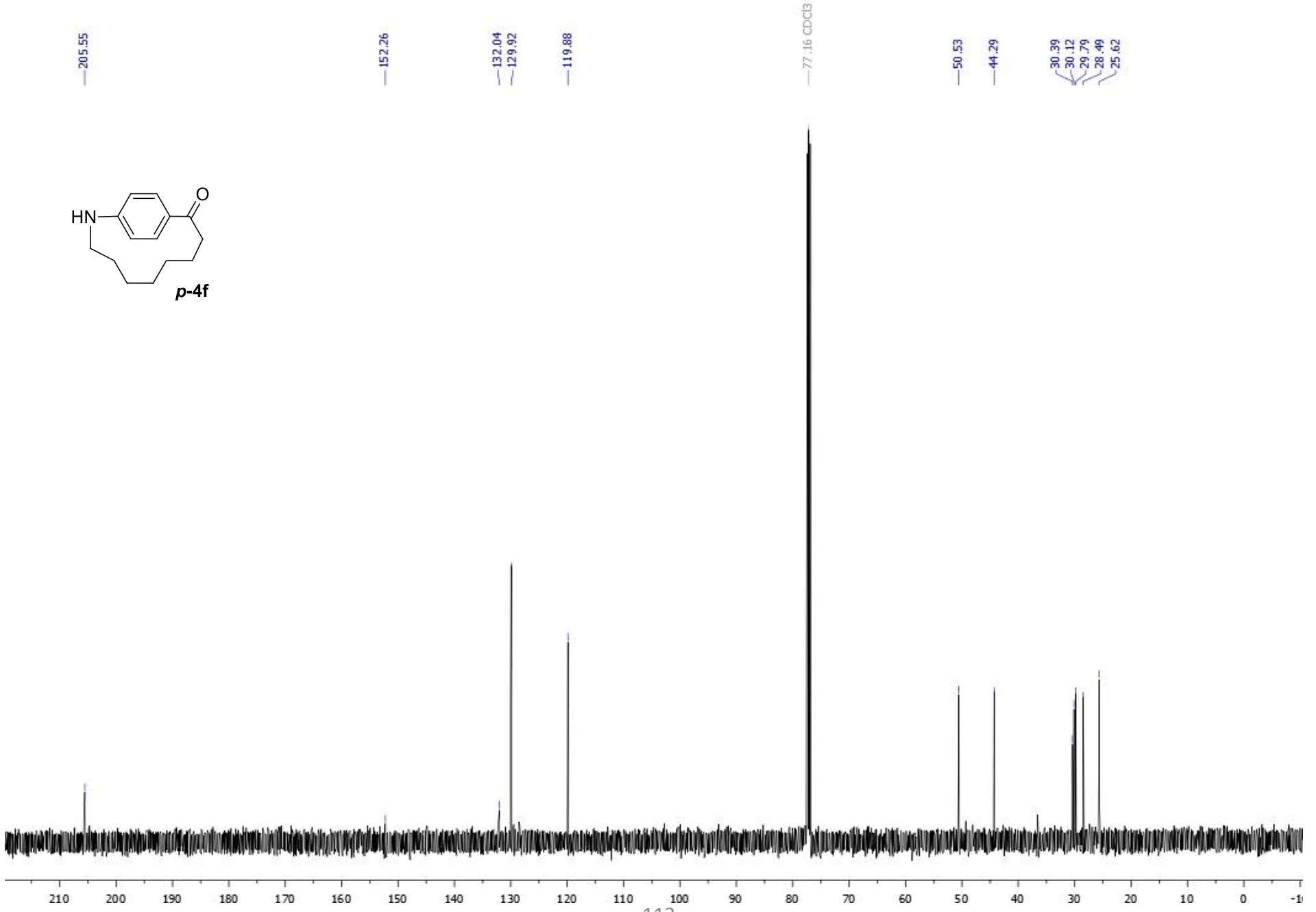
^{13}C NMR (126 MHz, Chloroform-*d*)



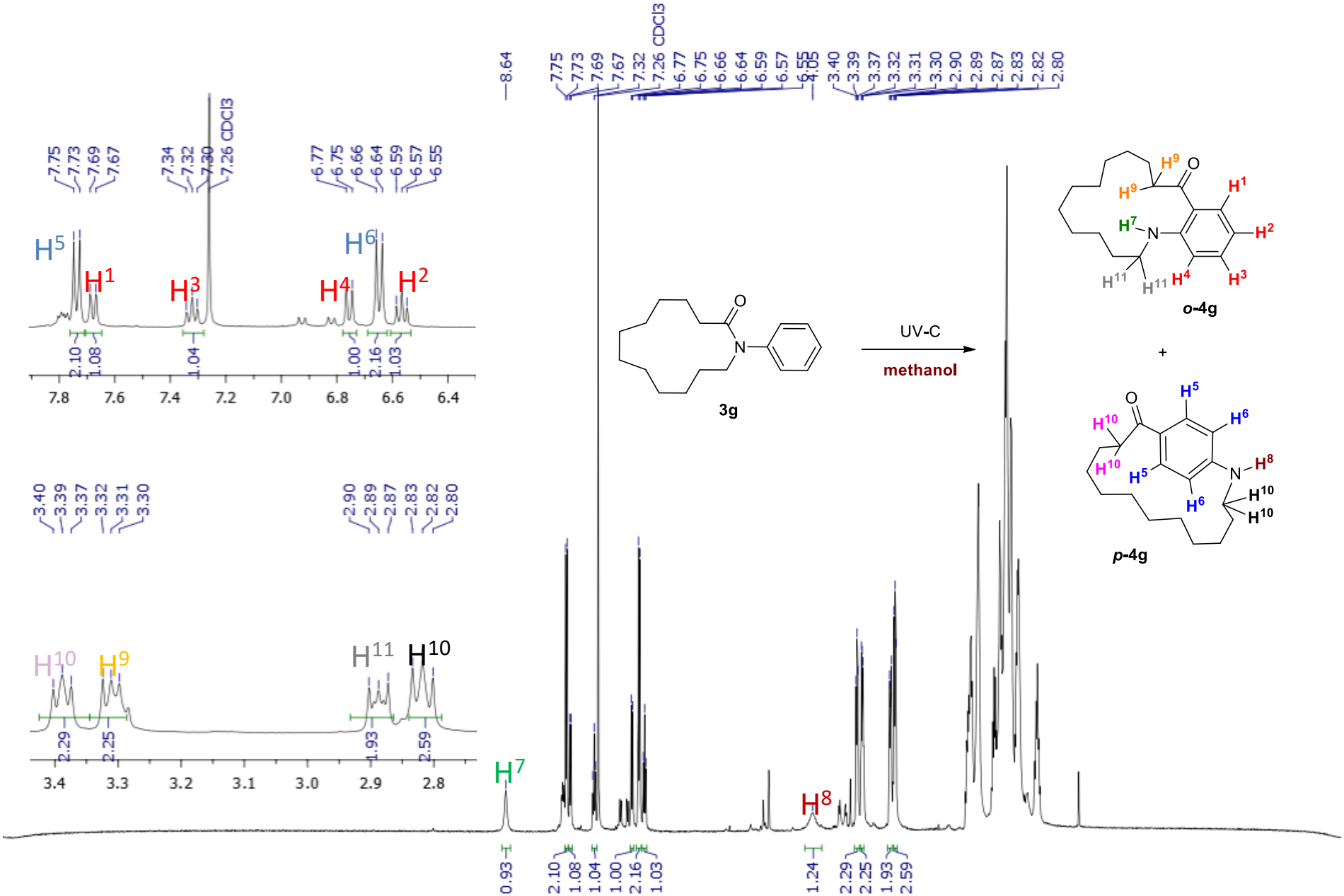
^{1}H NMR (600 MHz, Chloroform-*d*)



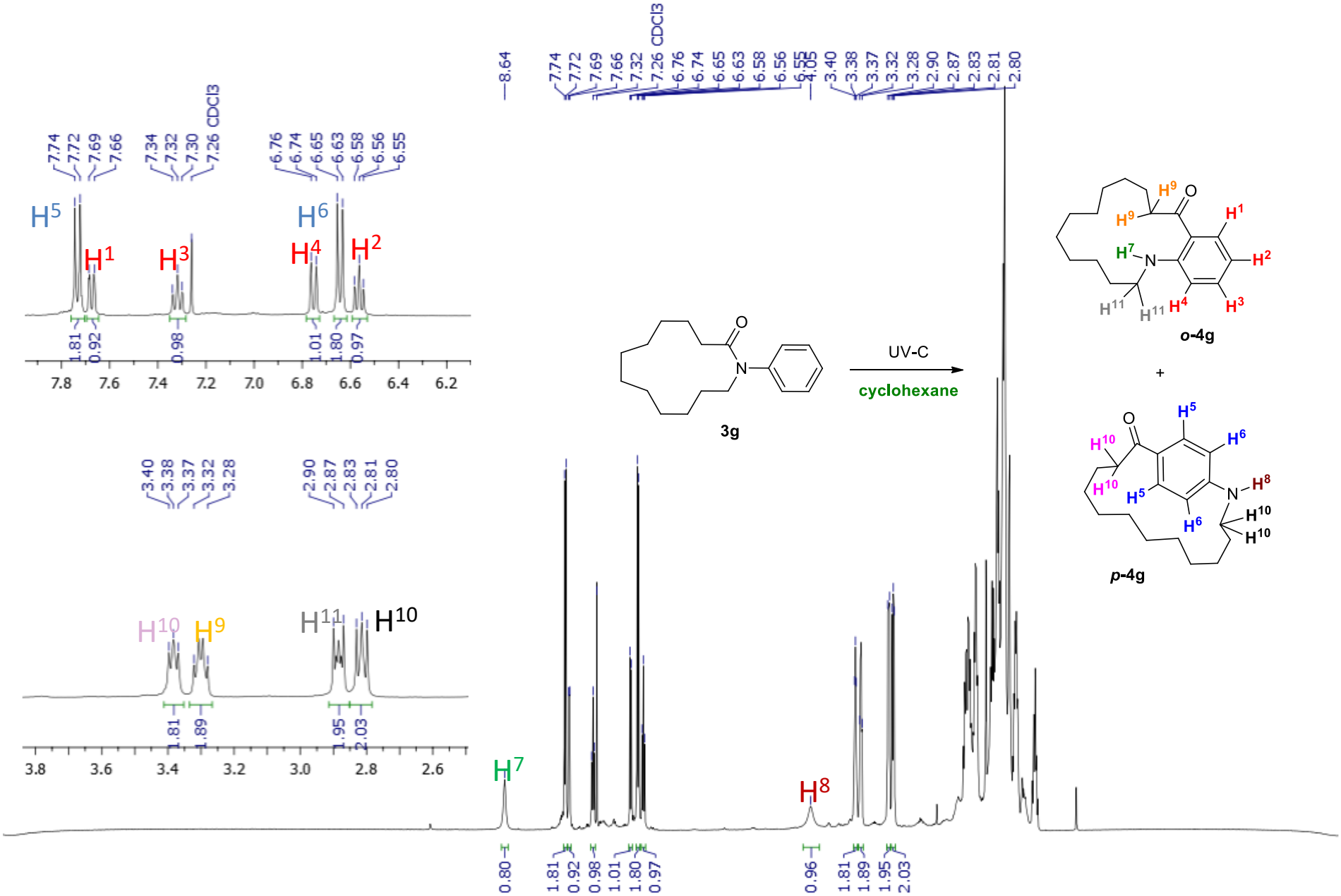
^{13}C NMR (126 MHz, Chloroform-*d*)



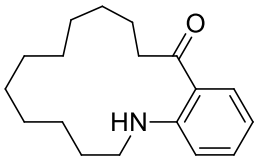
^{1}H NMR (400 MHz, Chloroform-*d*) of crude reaction mixture



^{1}H NMR (400 MHz, Chloroform-*d*) of crude reaction mixture

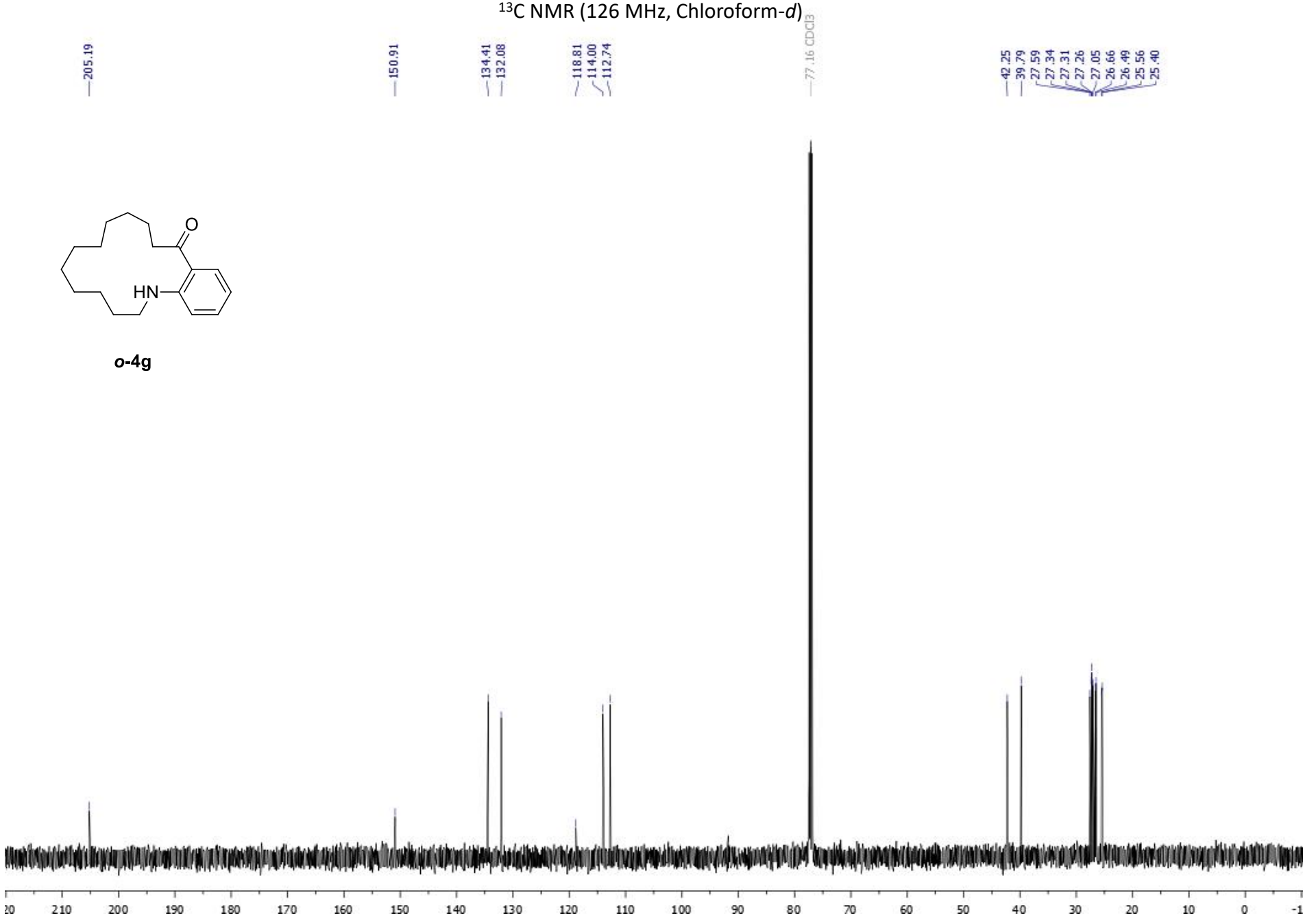


^{1}H NMR (500 MHz, Chloroform-*d*)



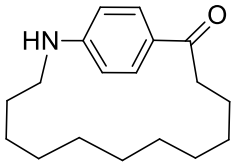
***o*-4g**

^{13}C NMR (126 MHz, Chloroform-*d*)



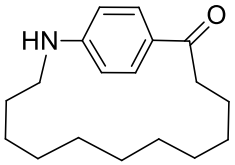
***o*-4g**

^{1}H NMR (500 MHz, Chloroform-*d*)

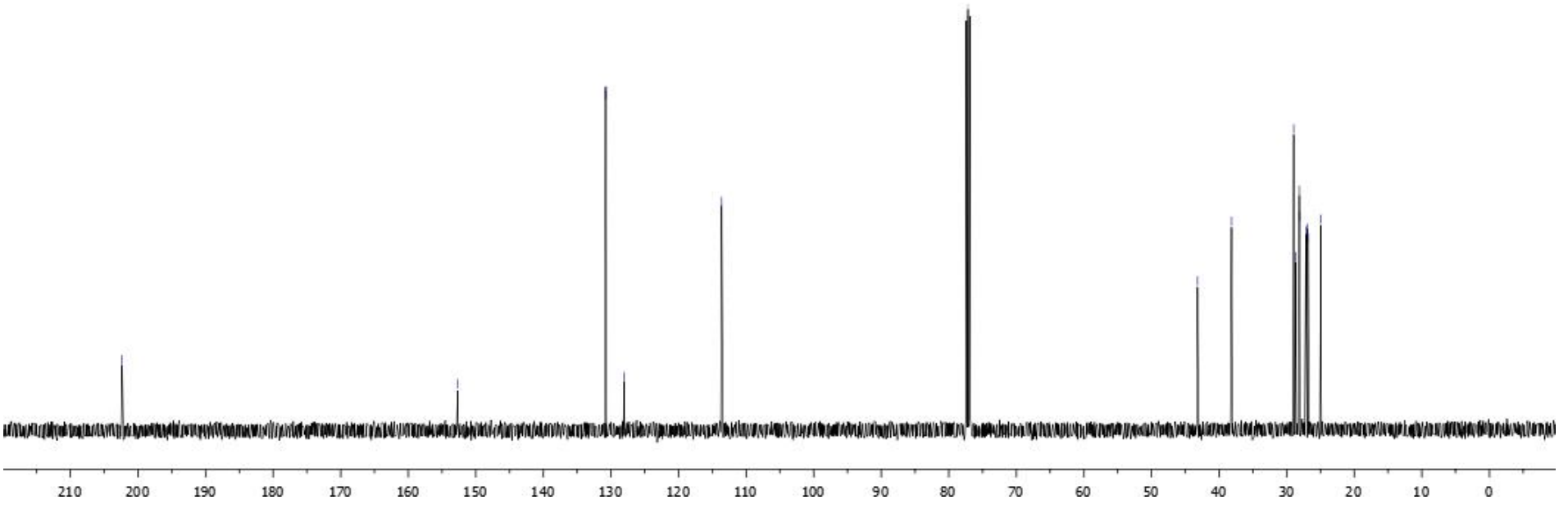


***p*-4g**

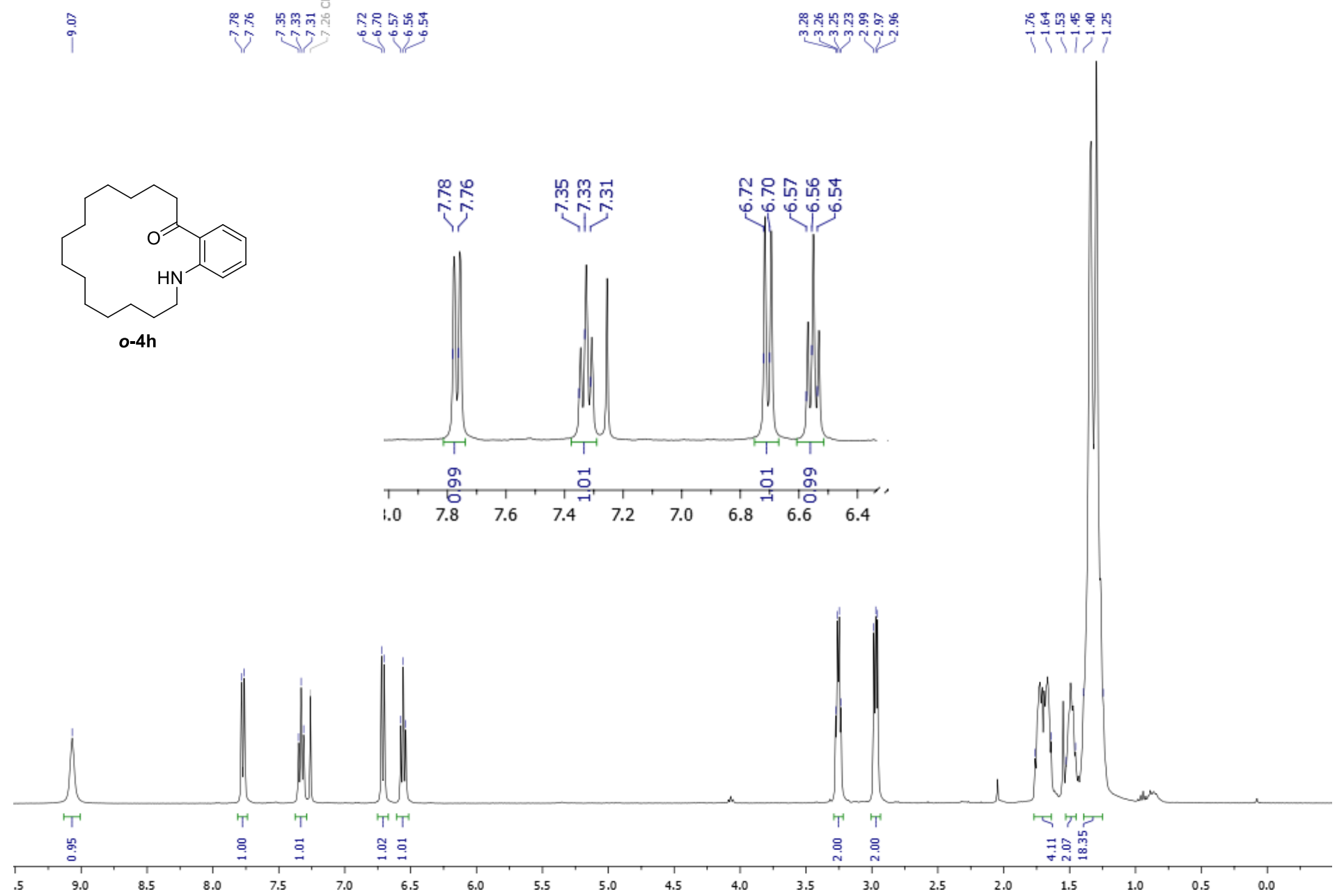
^{13}C NMR (126 MHz, Chloroform-*d*)



***p*-4g**

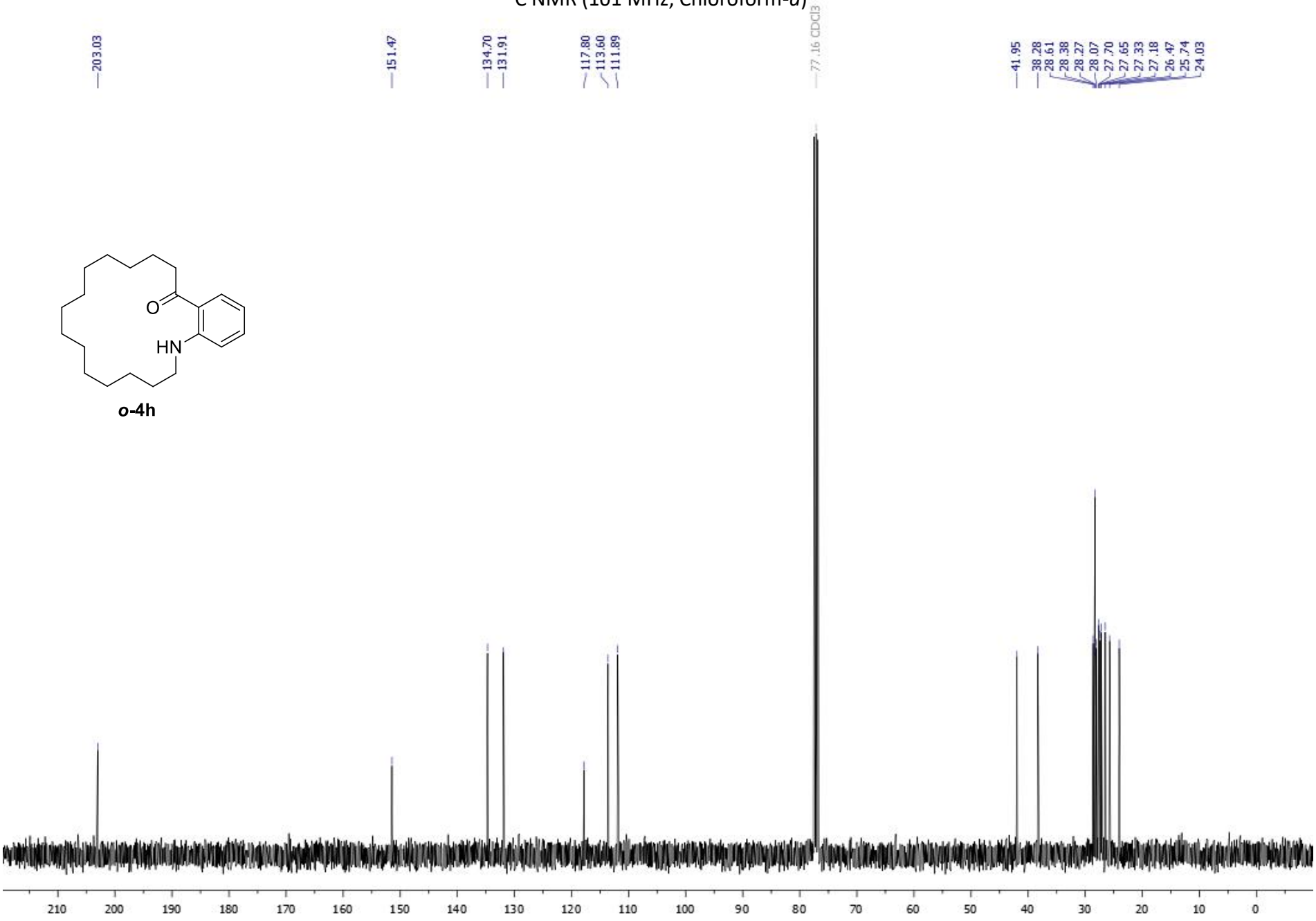


^{1}H NMR (400 MHz, Chloroform-*d*)



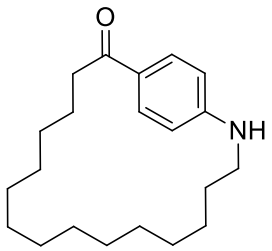
***o*-4h**

^{13}C NMR (101 MHz, Chloroform-*d*)



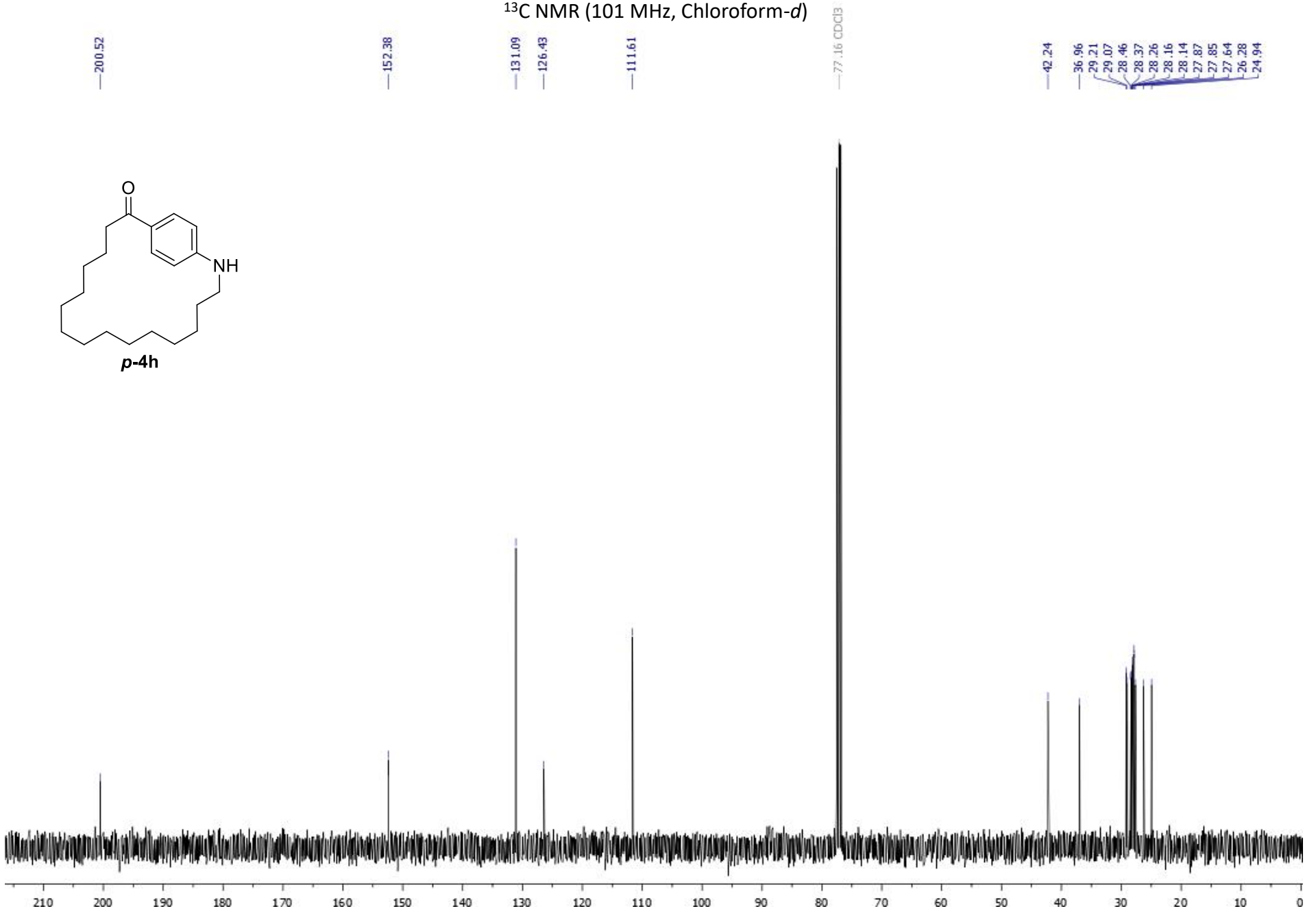
***o*-4h**

^{1}H NMR (400 MHz, Chloroform-*d*)



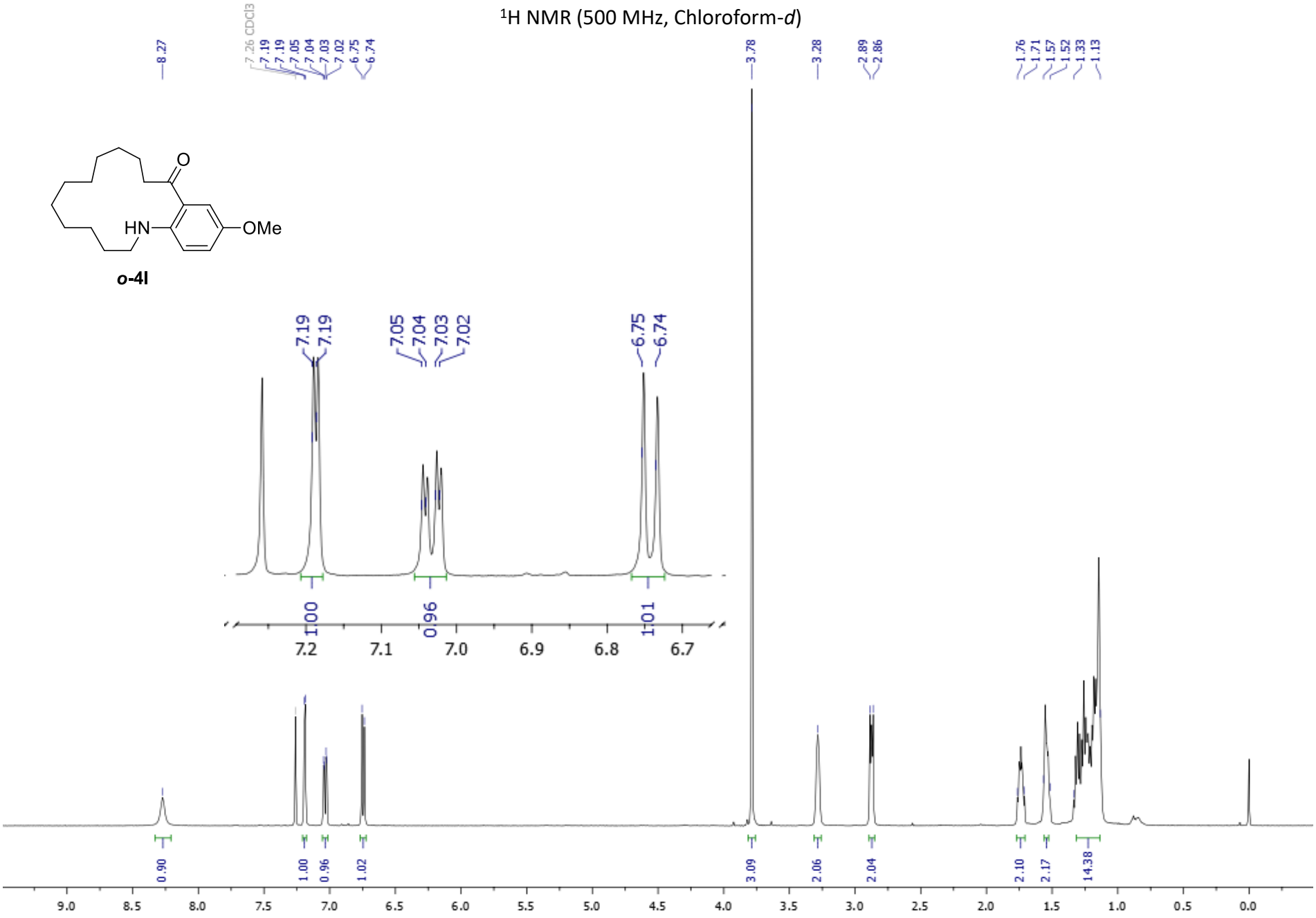
***p*-4h**

^{13}C NMR (101 MHz, Chloroform-*d*)



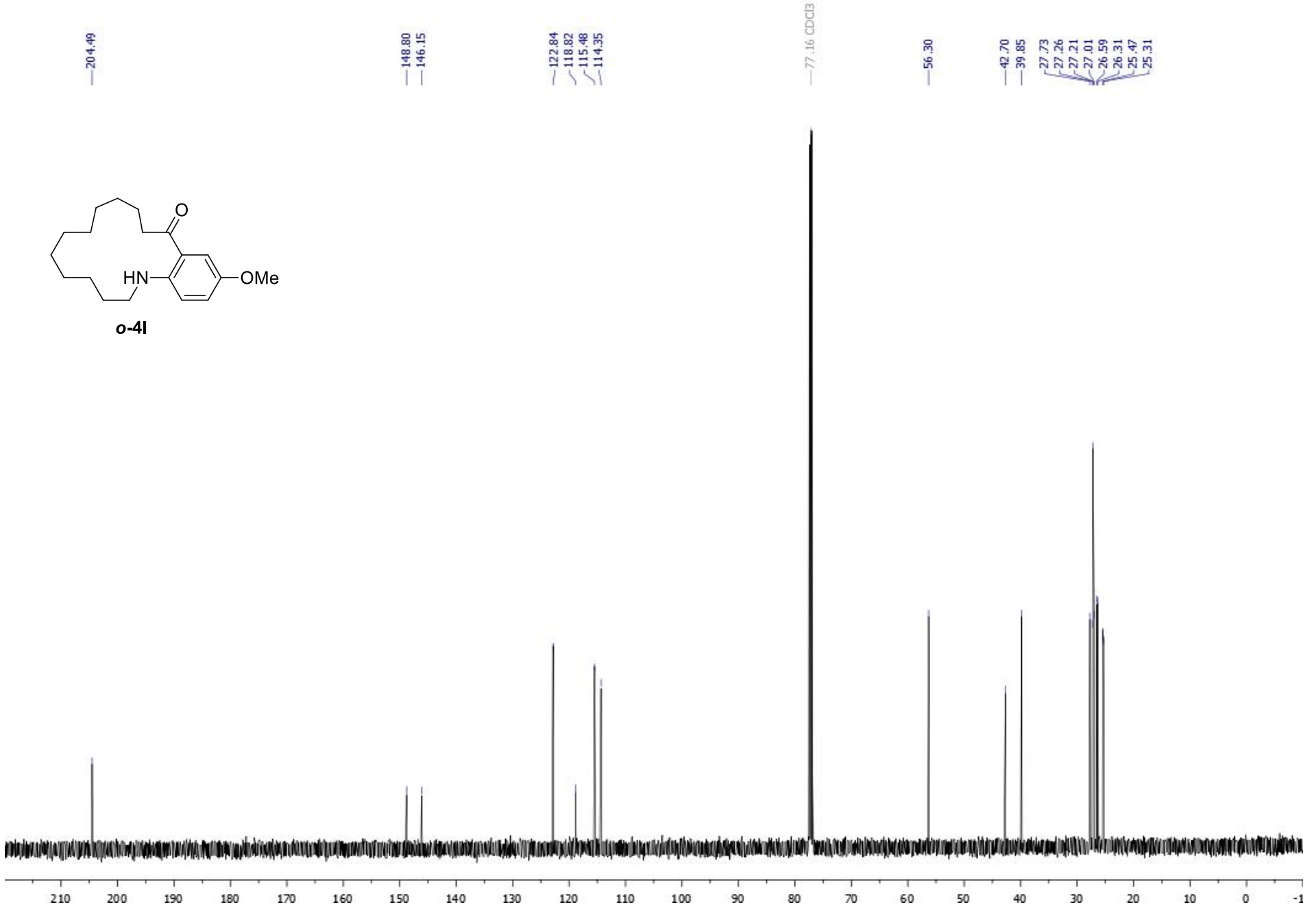
***p*-4h**

^{1}H NMR (500 MHz, Chloroform-*d*)



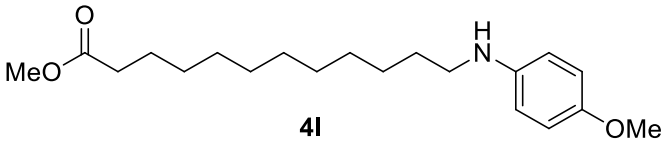
***o*-4l**

^{13}C NMR (126 MHz, Chloroform-*d*)



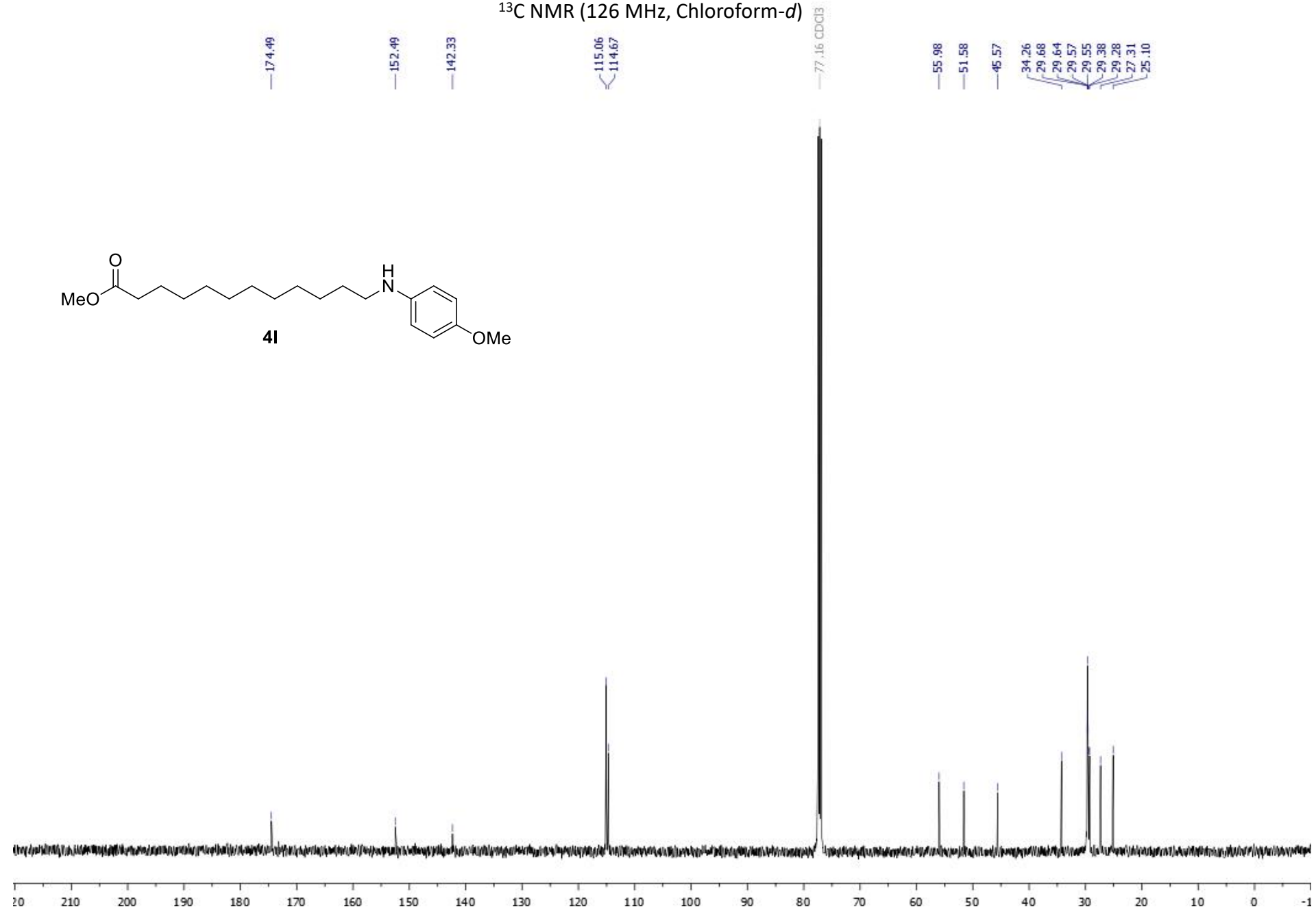
***o*-4l**

^{1}H NMR (600 MHz, Chloroform-*d*)

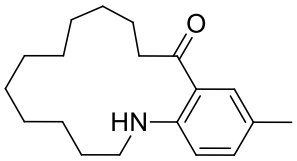


4l

^{13}C NMR (126 MHz, Chloroform-*d*)

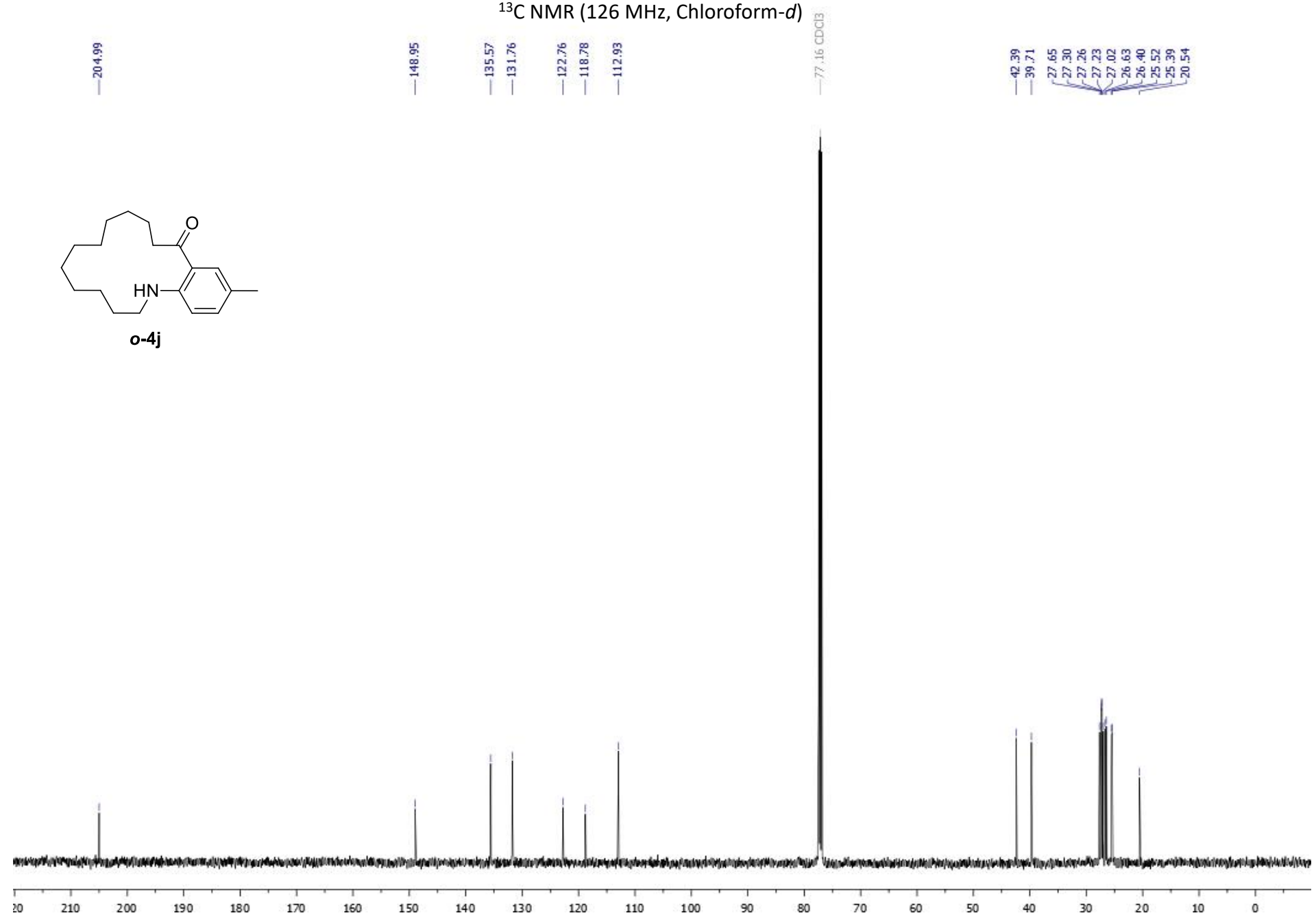


^{1}H NMR (500 MHz, Chloroform-*d*)

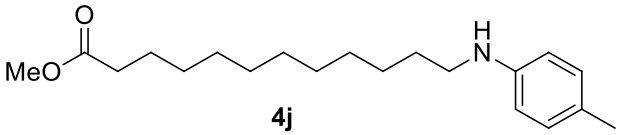


***o*-4j**

^{13}C NMR (126 MHz, Chloroform-*d*)

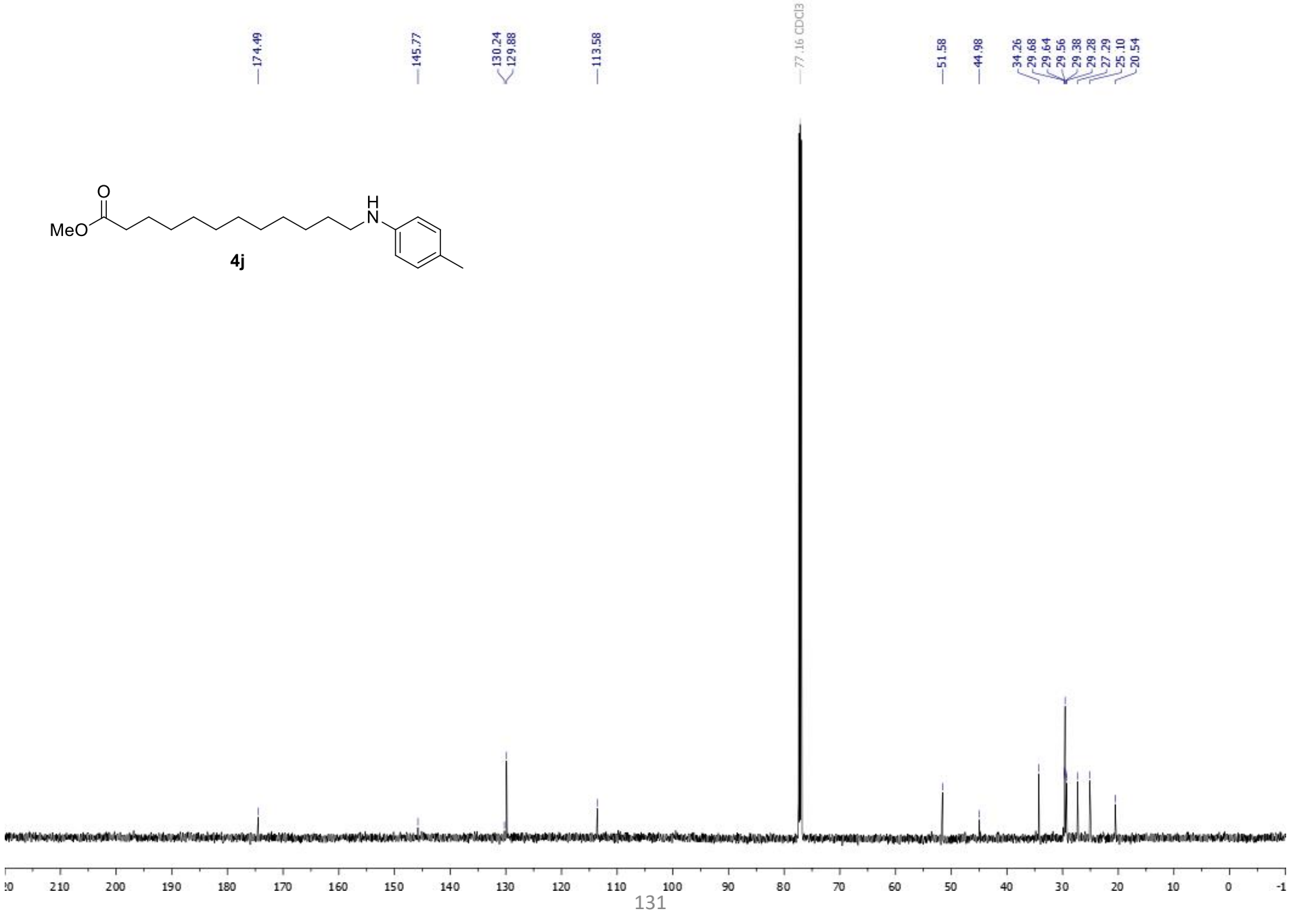


^{1}H NMR (600 MHz, Chloroform-*d*)

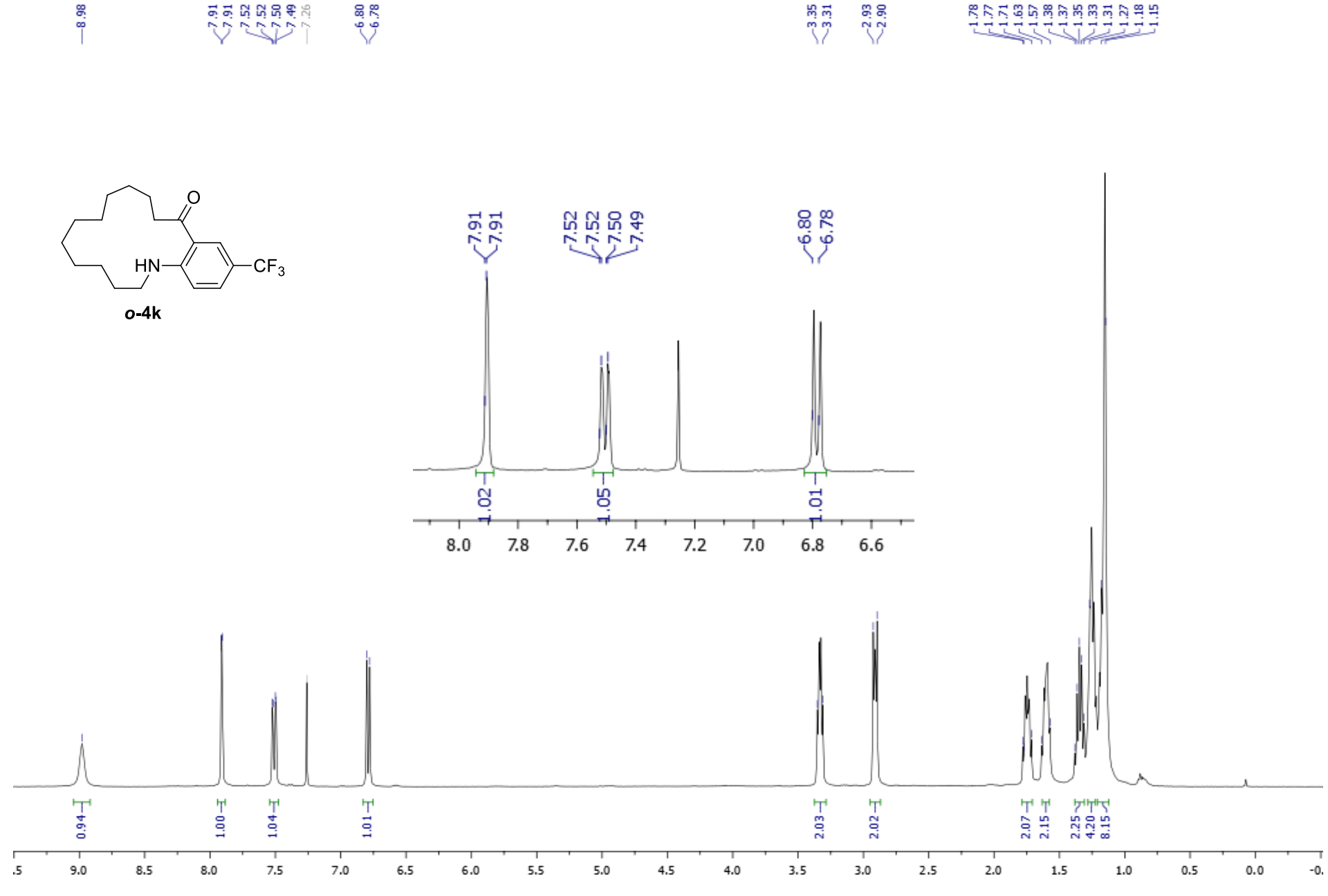


4j

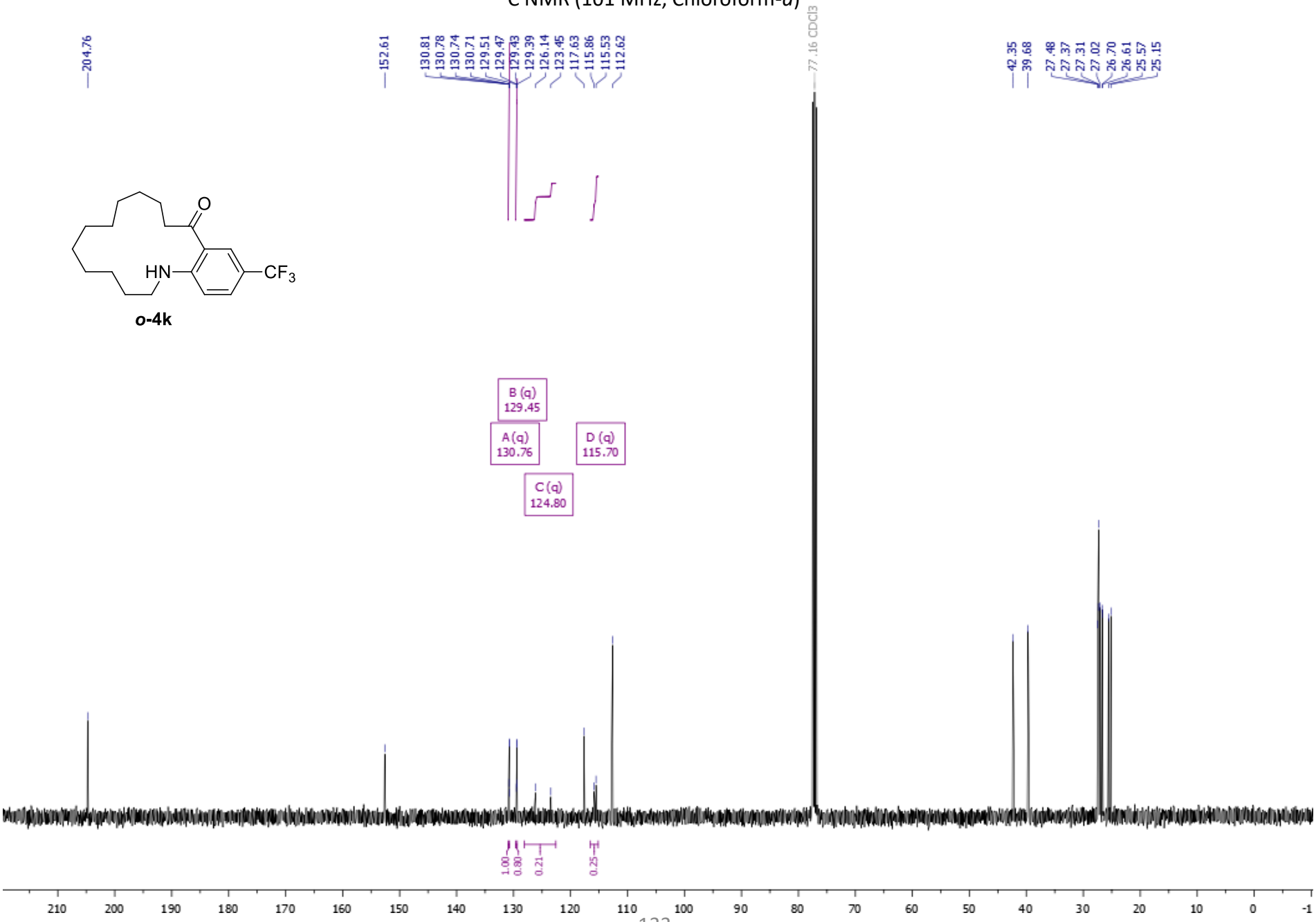
^{13}C NMR (151 MHz, Chloroform-*d*)



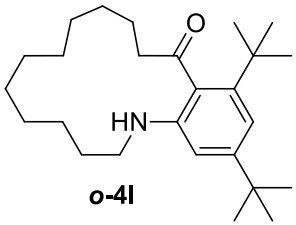
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

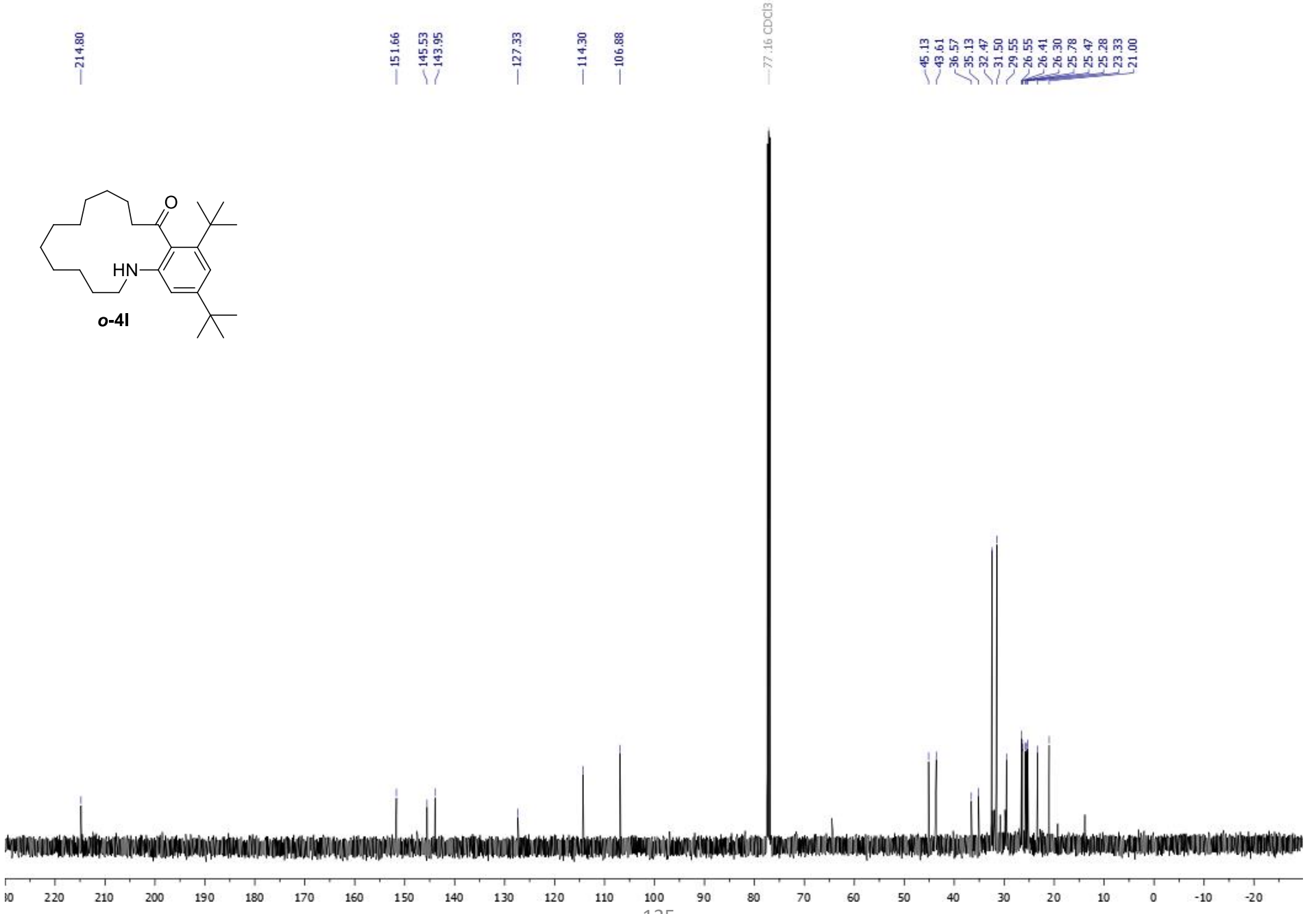


^{1}H NMR (500 MHz, Chloroform-*d*)

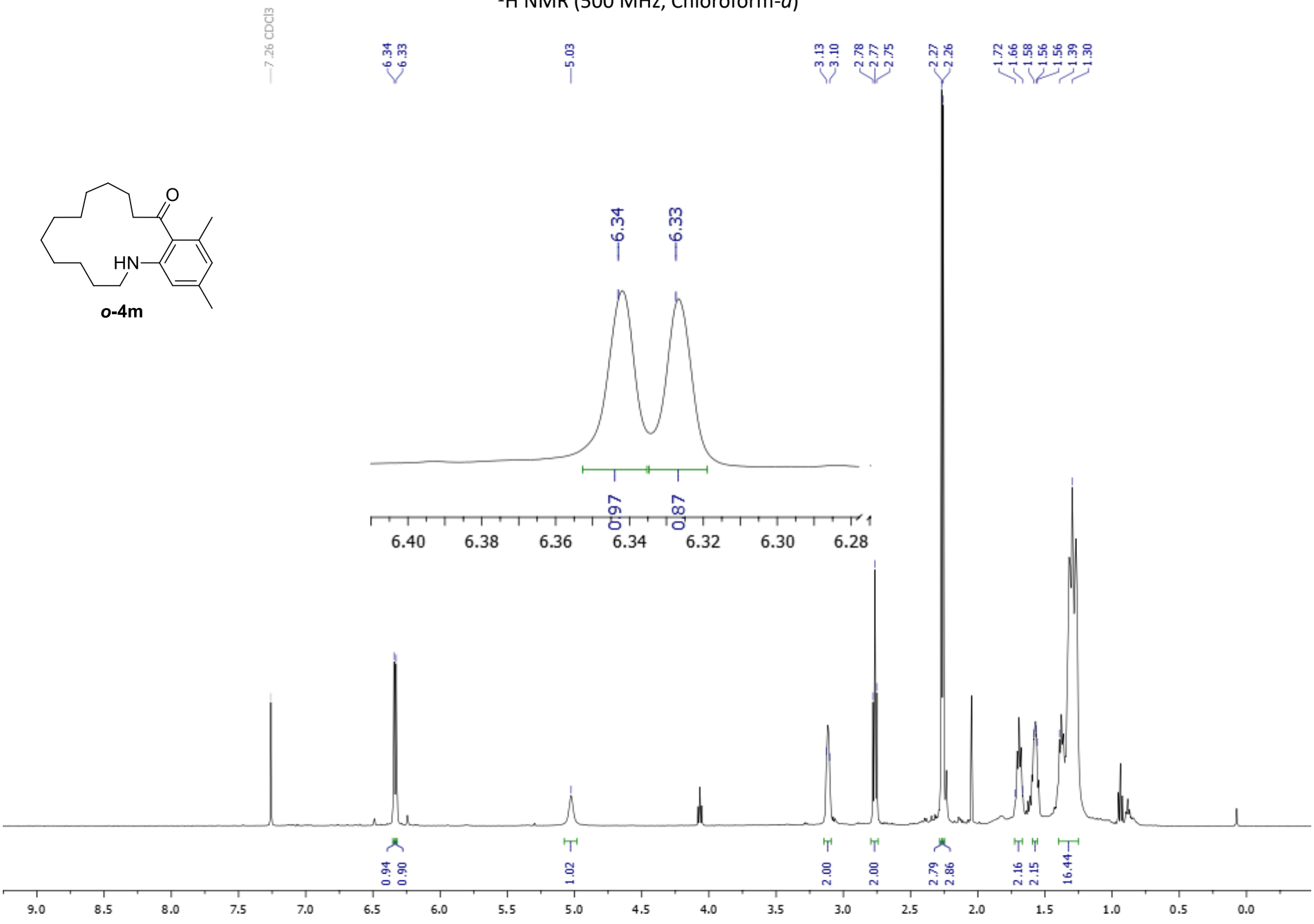


***o*-4l**

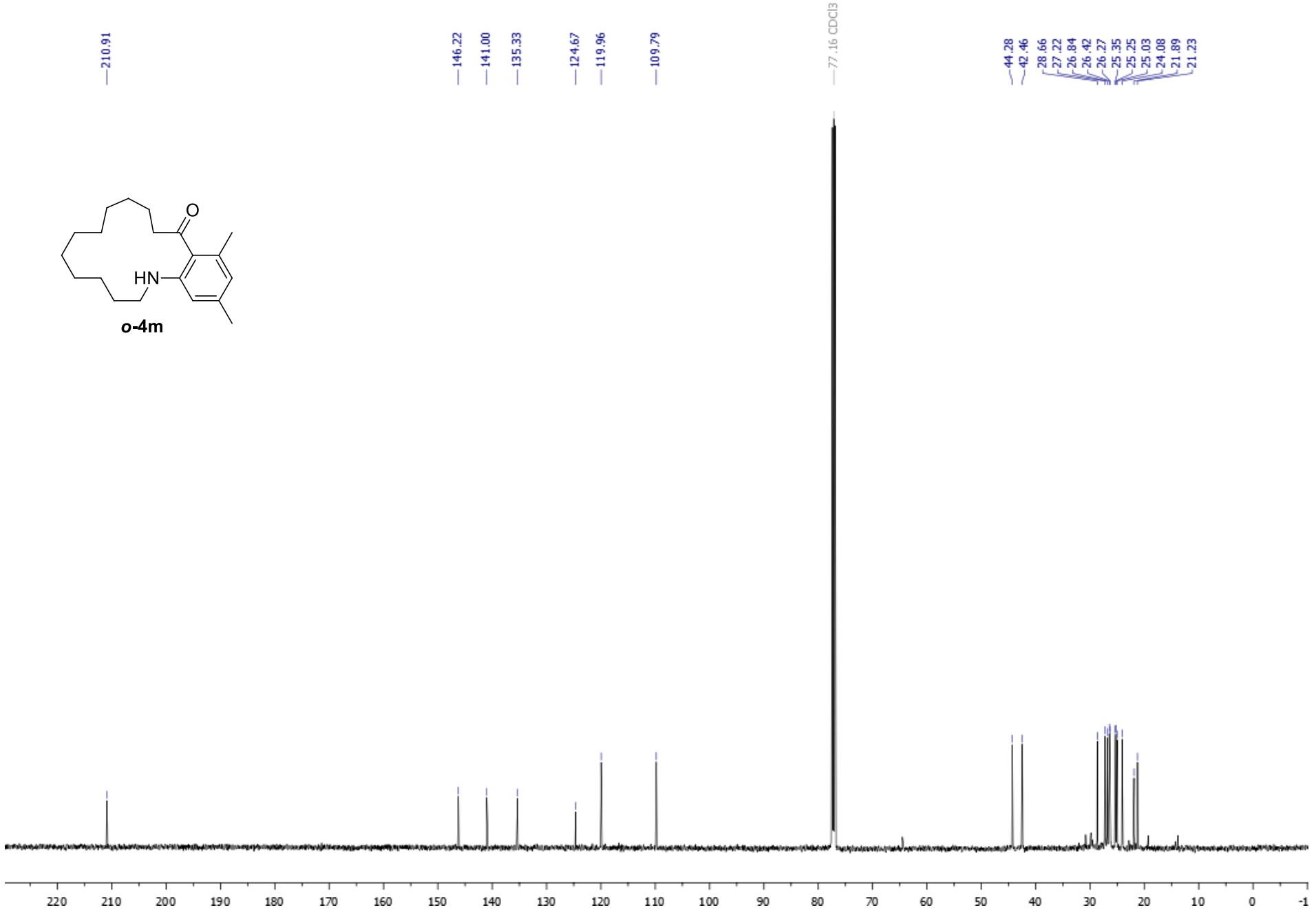
^{13}C NMR (126 MHz, Chloroform-*d*)



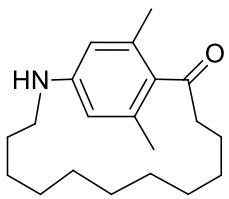
^{1}H NMR (500 MHz, Chloroform-*d*)



^{13}C NMR (126 MHz, Chloroform-*d*)

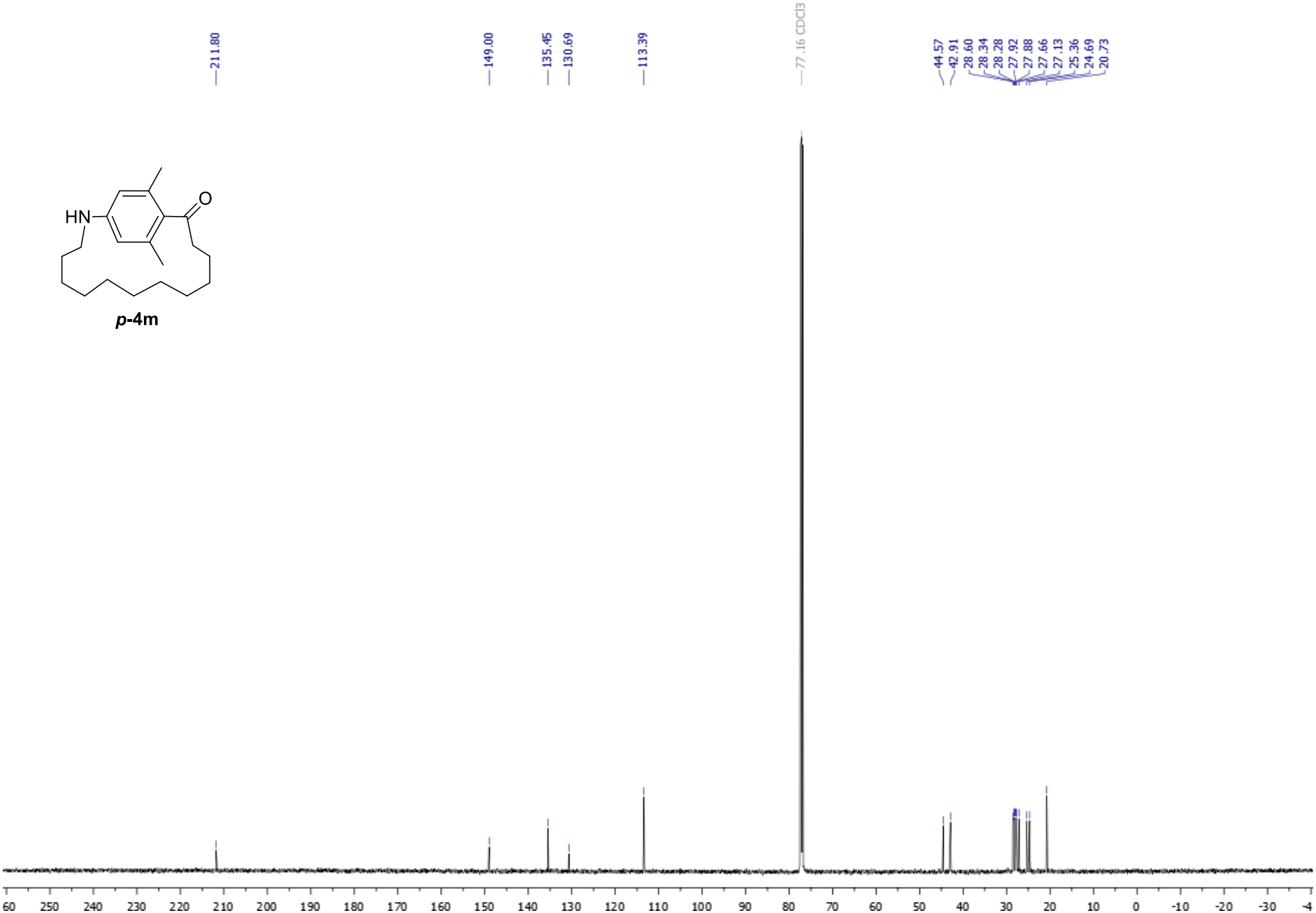


^{1}H NMR (500 MHz, Chloroform-*d*)



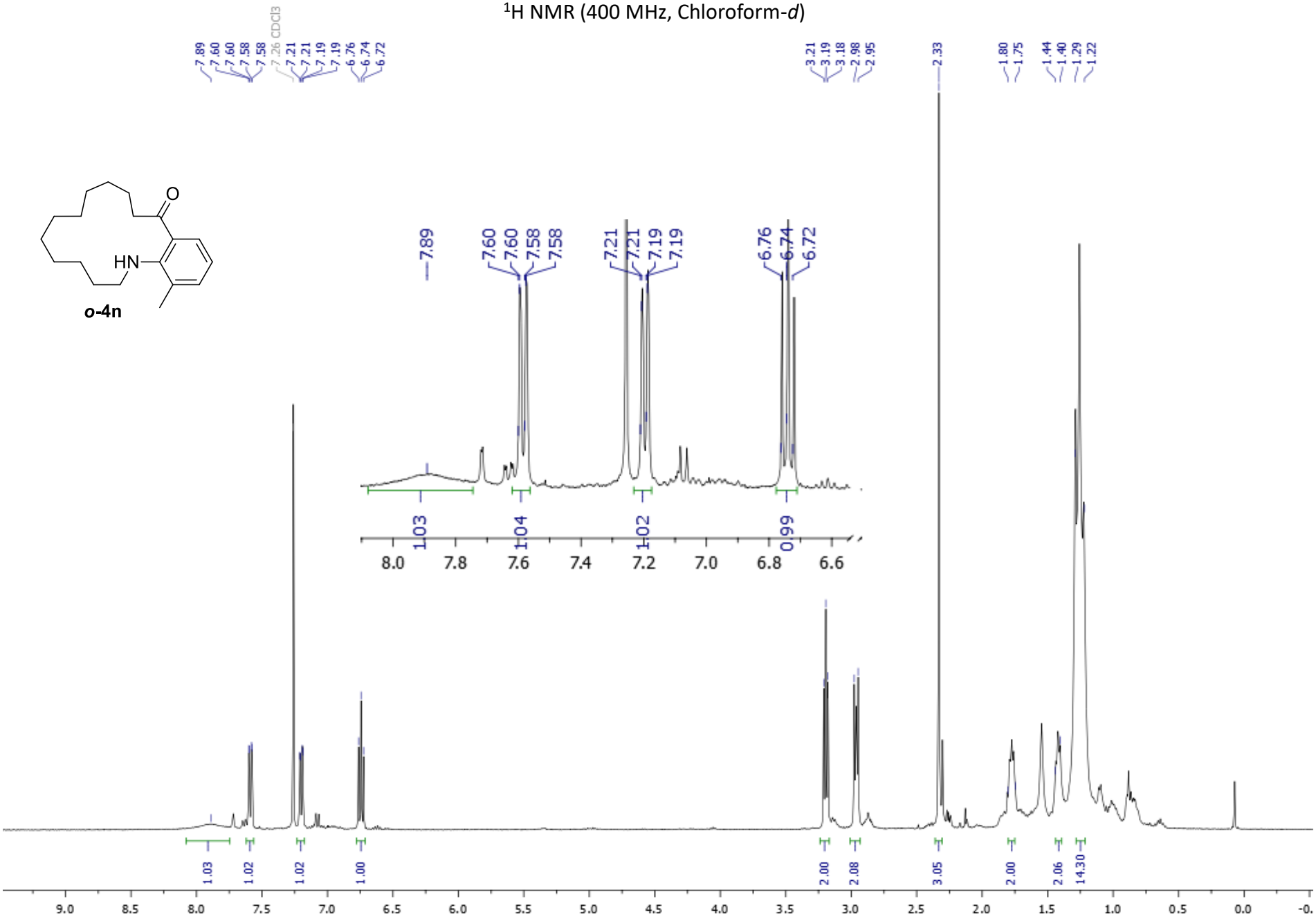
***p*-4m**

^{13}C NMR (126 MHz, Chloroform-*d*)

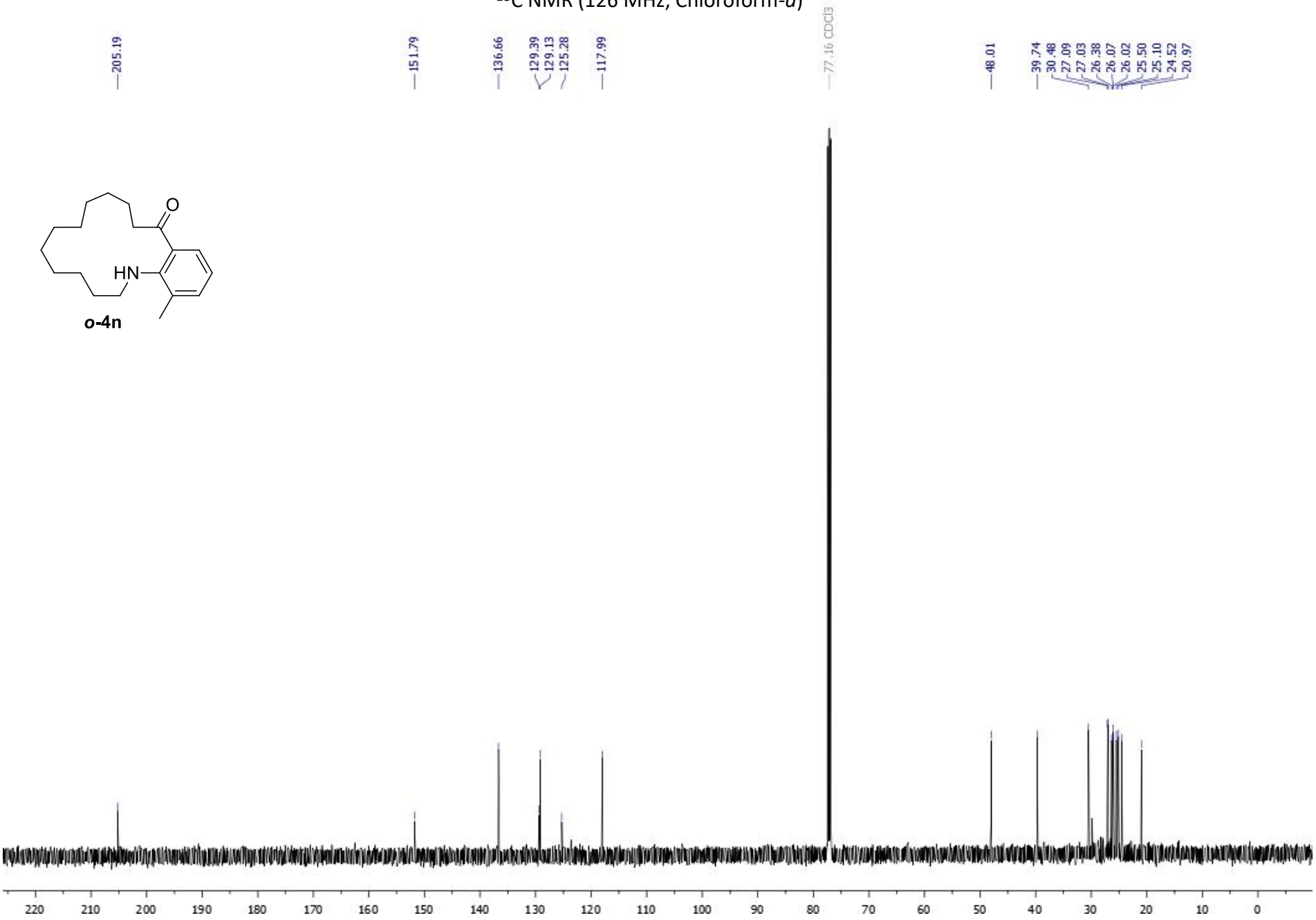


***p*-4m**

^{1}H NMR (400 MHz, Chloroform-*d*)

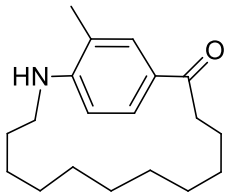


^{13}C NMR (126 MHz, Chloroform-*d*)



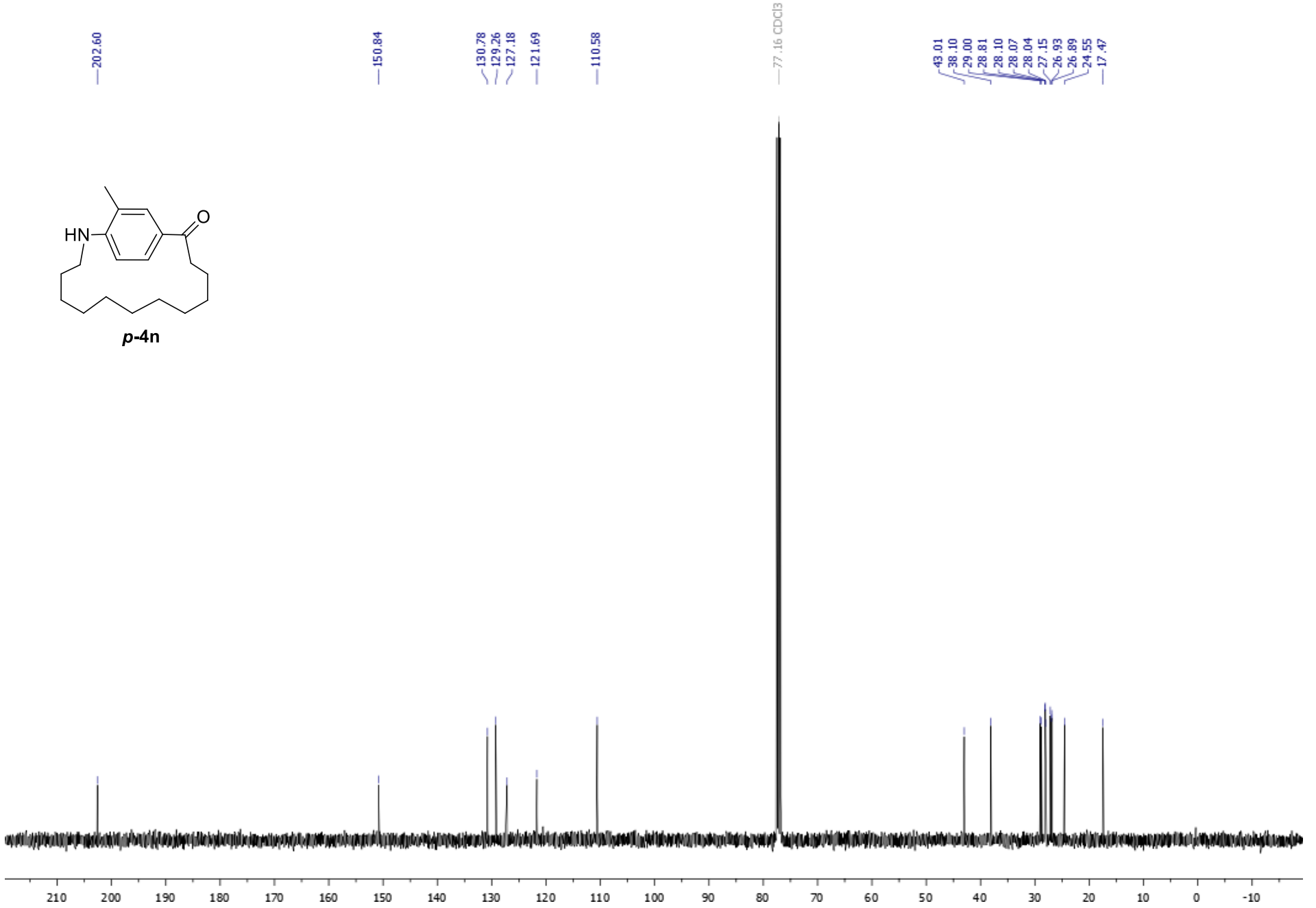
***o*-4n**

^{1}H NMR (400 MHz, Chloroform-*d*)



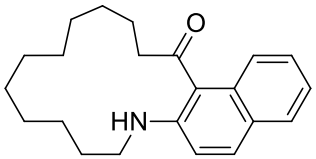
***p*-4n**

^{13}C NMR (101 MHz, Chloroform-*d*)



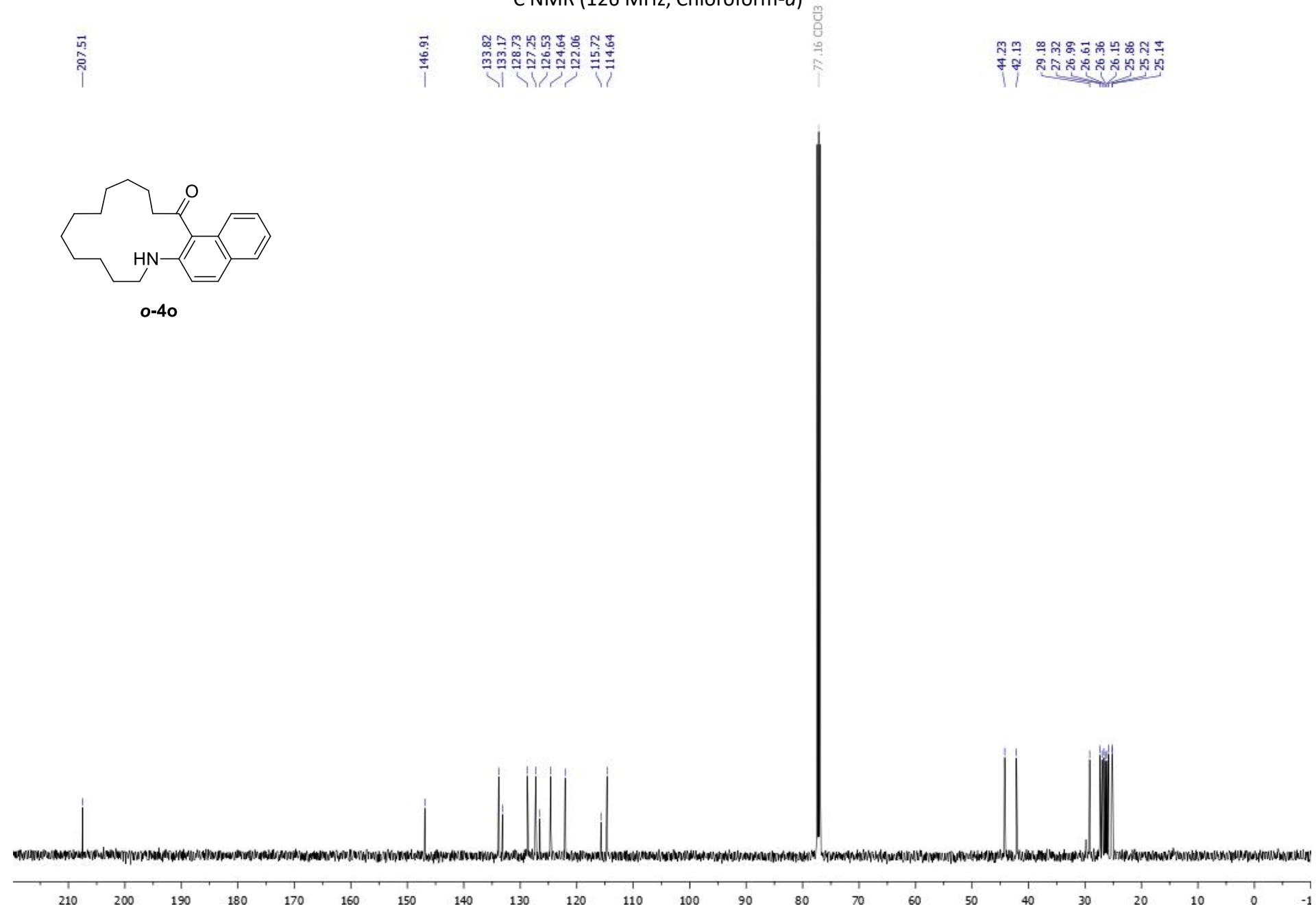
***p*-4n**

^{1}H NMR (500 MHz, Benzene-d_6)



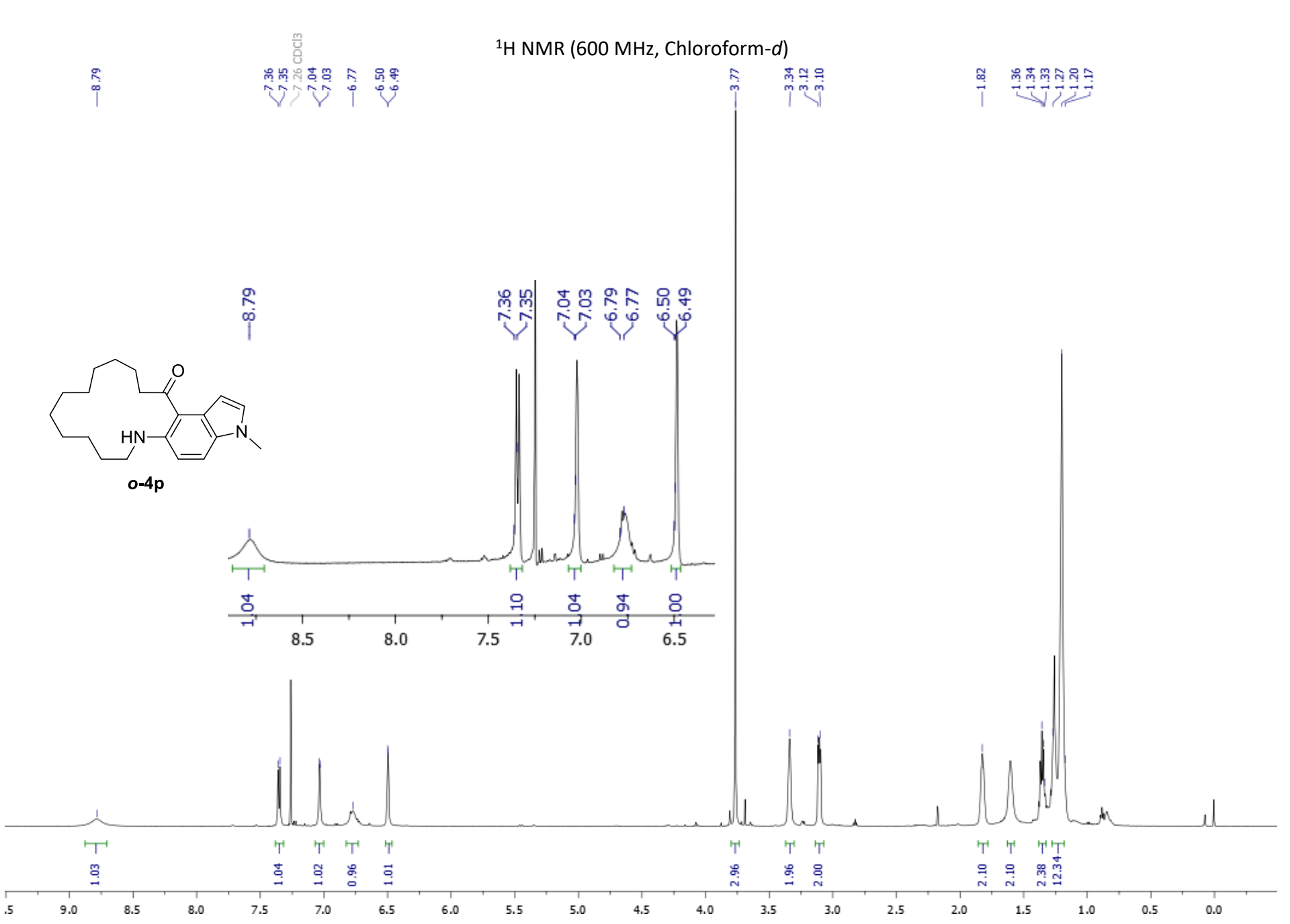
***o*-4o**

^{13}C NMR (126 MHz, Chloroform-*d*)

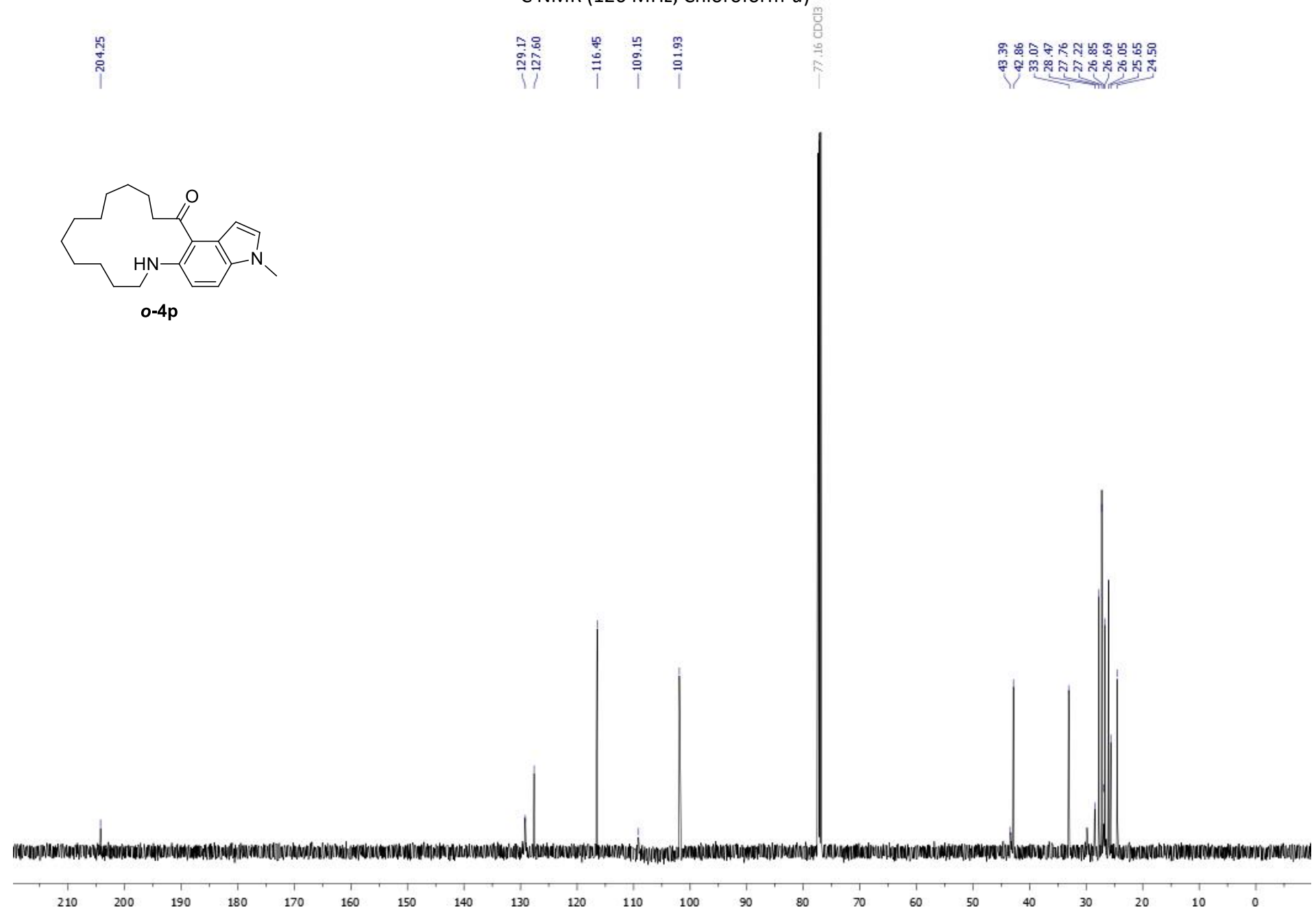


***o*-4o**

^{1}H NMR (600 MHz, Chloroform-*d*)

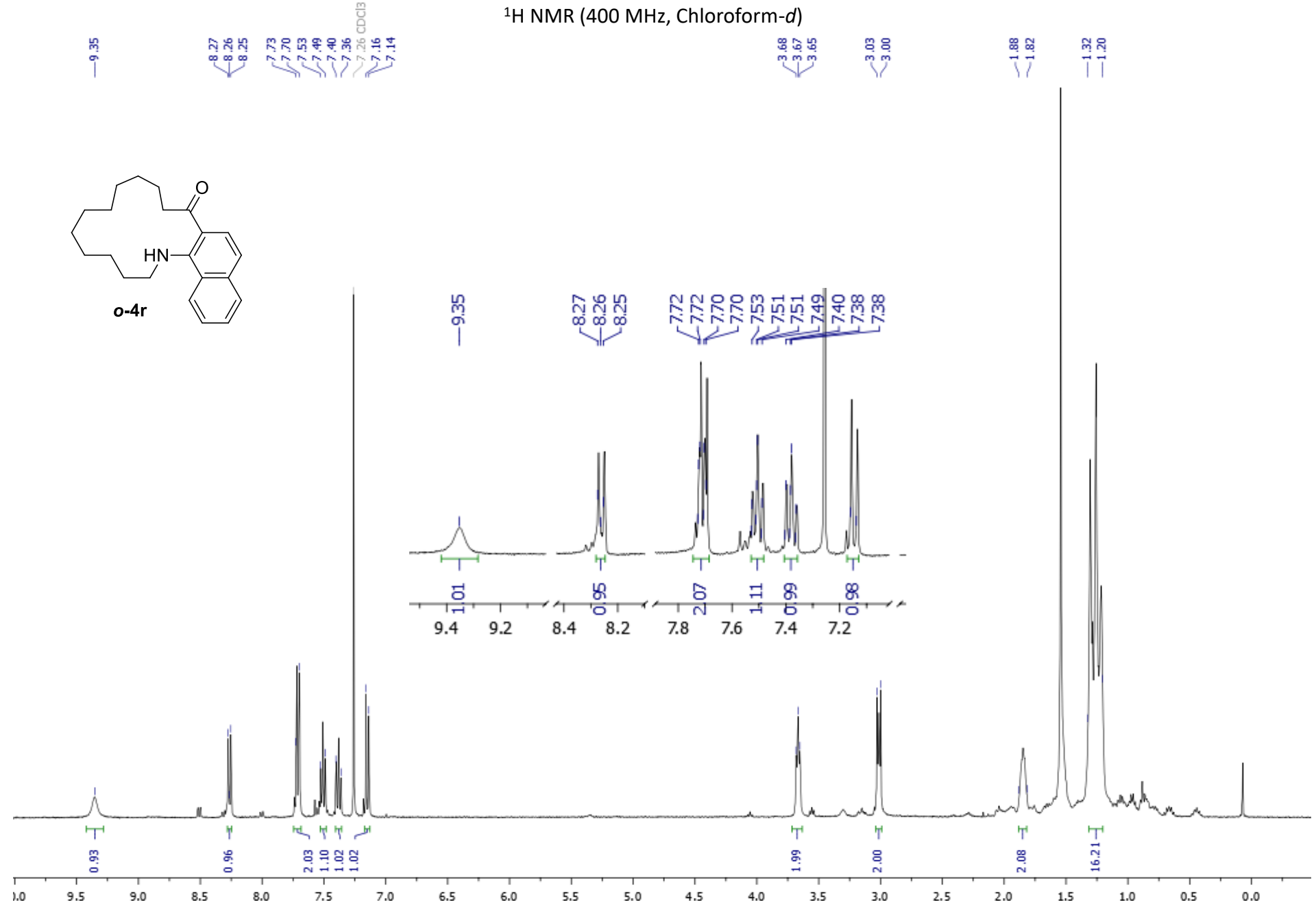


^{13}C NMR (126 MHz, Chloroform-*d*)

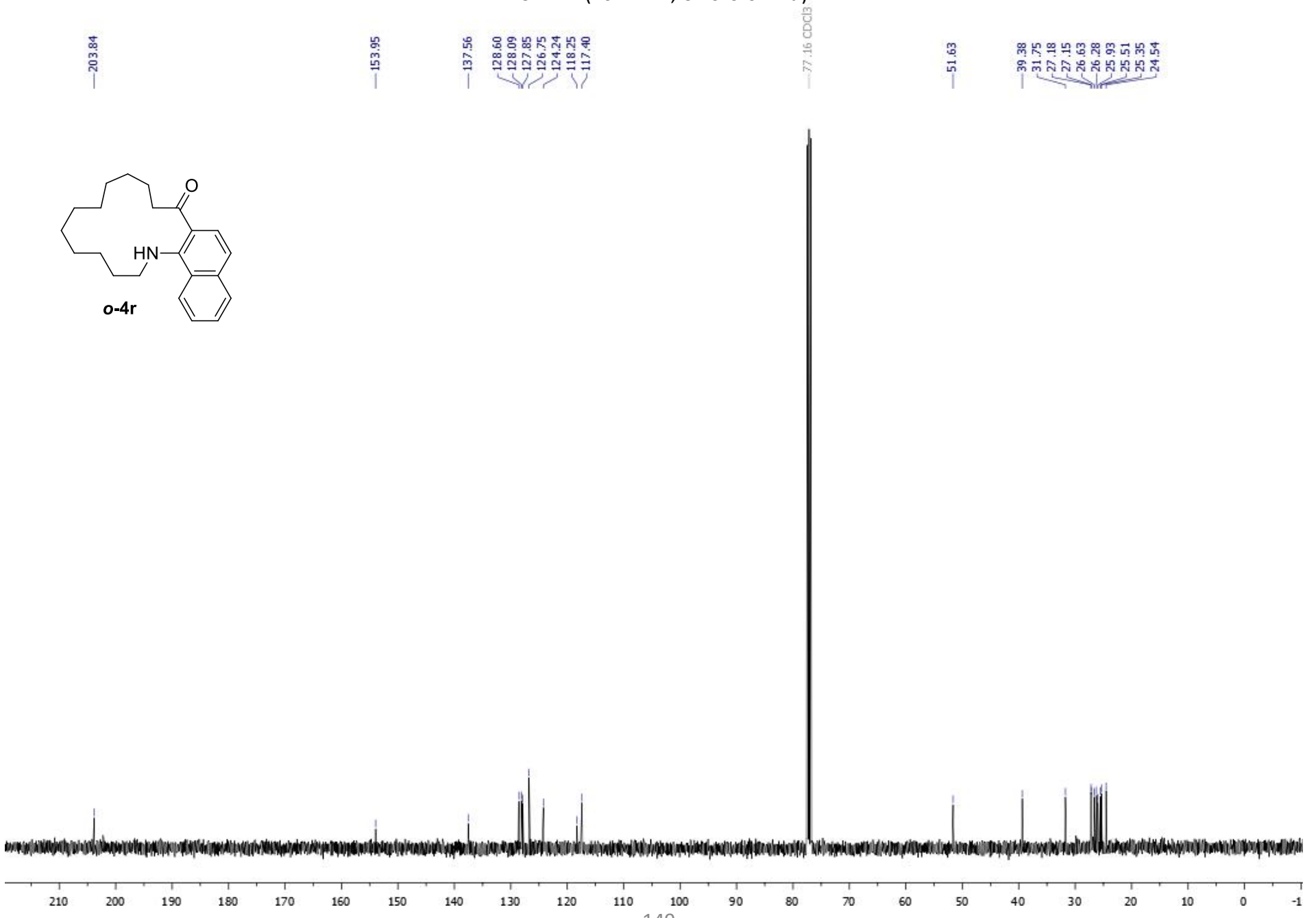


***o*-4p**

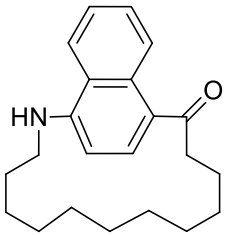
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)

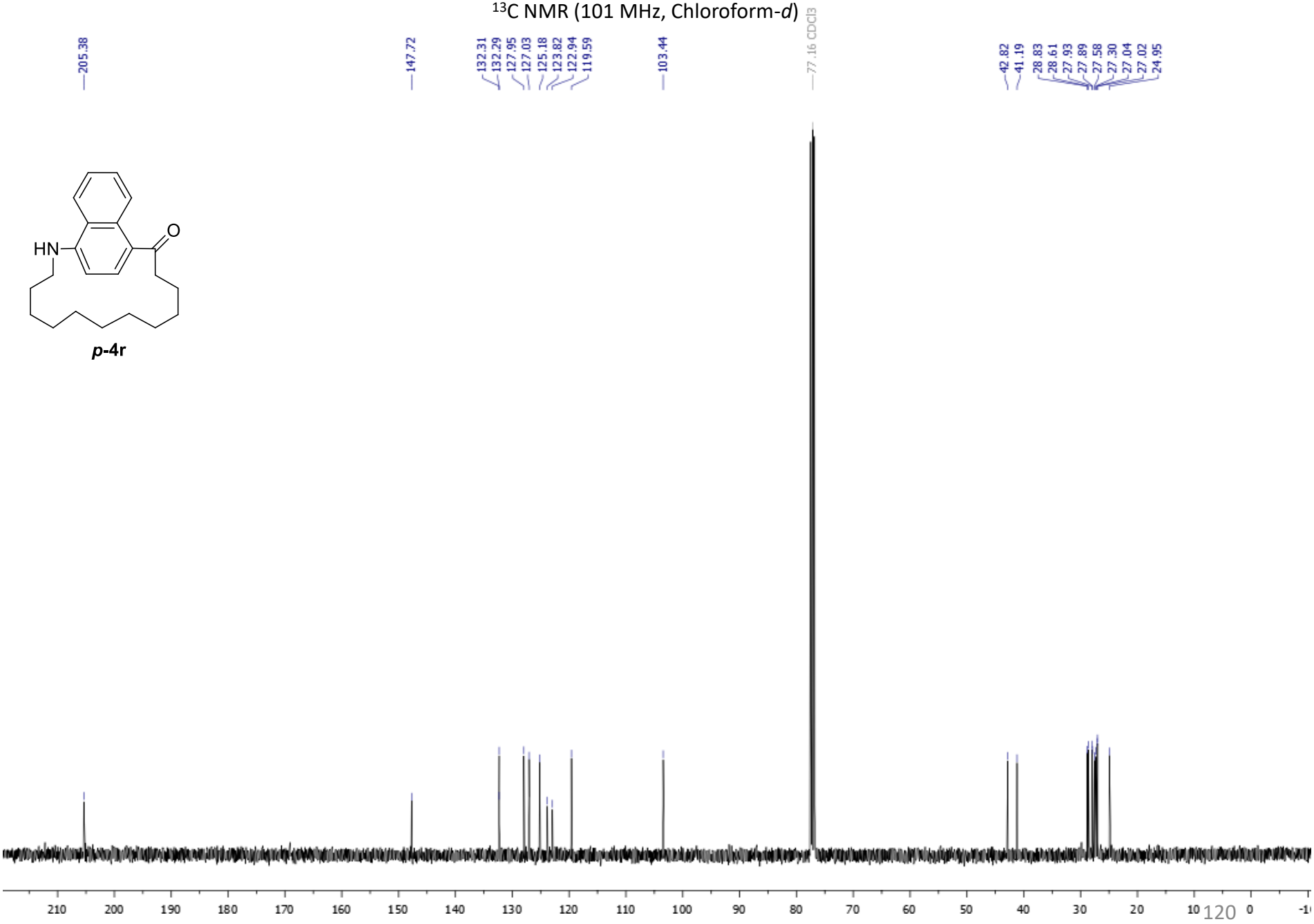


^{1}H NMR (400 MHz, Chloroform-*d*)



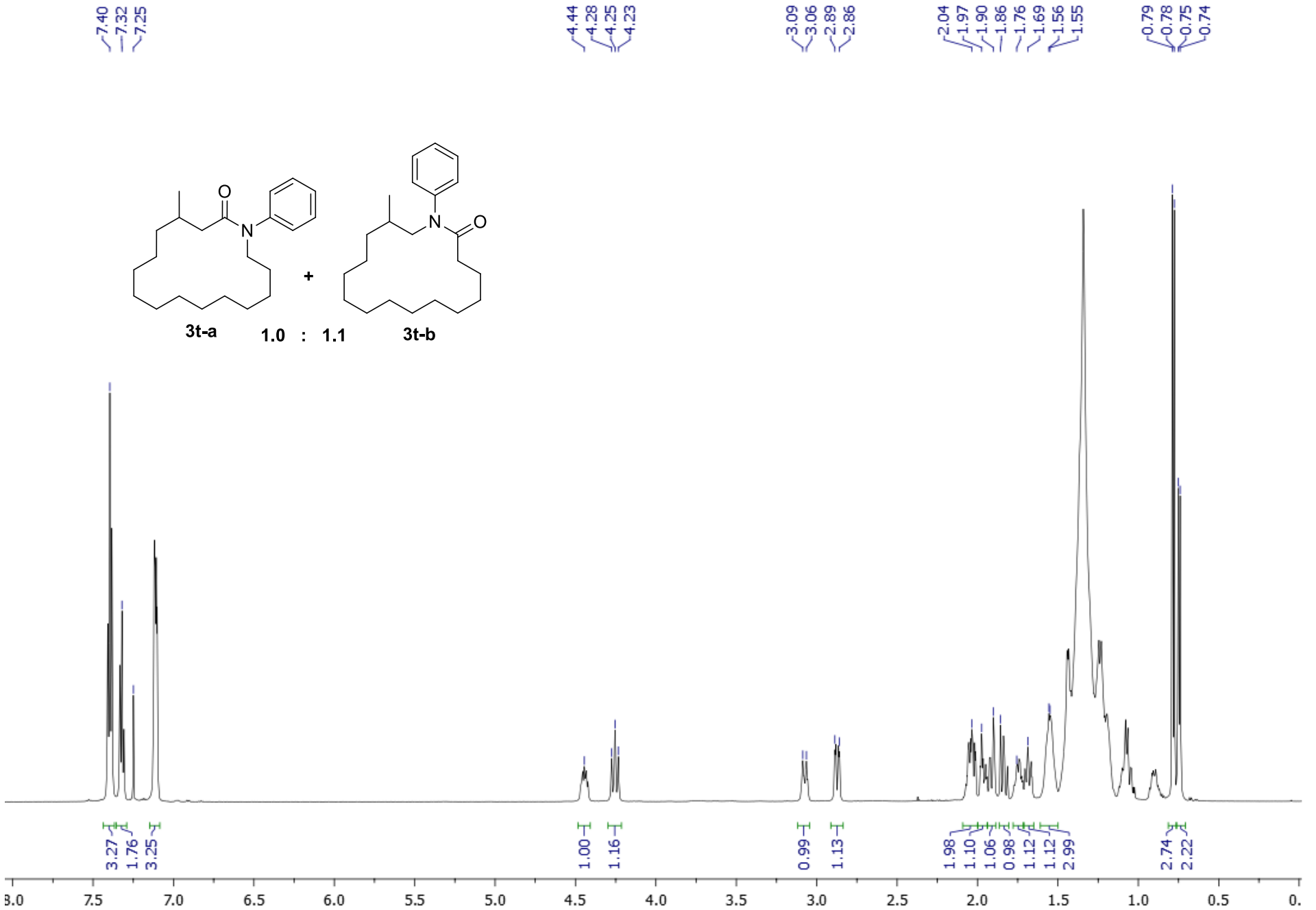
***p*-4r**

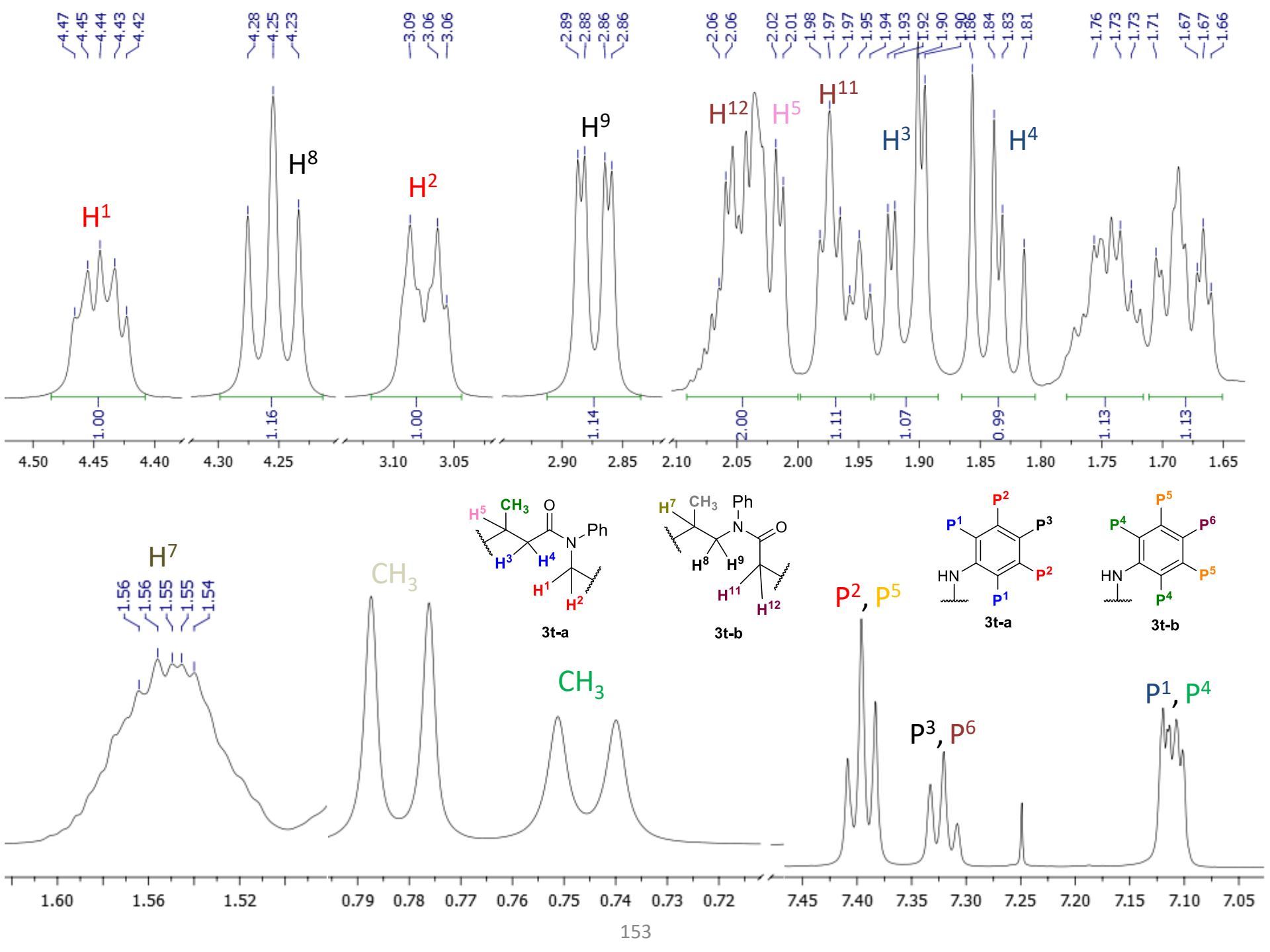
^{13}C NMR (101 MHz, Chloroform-*d*)



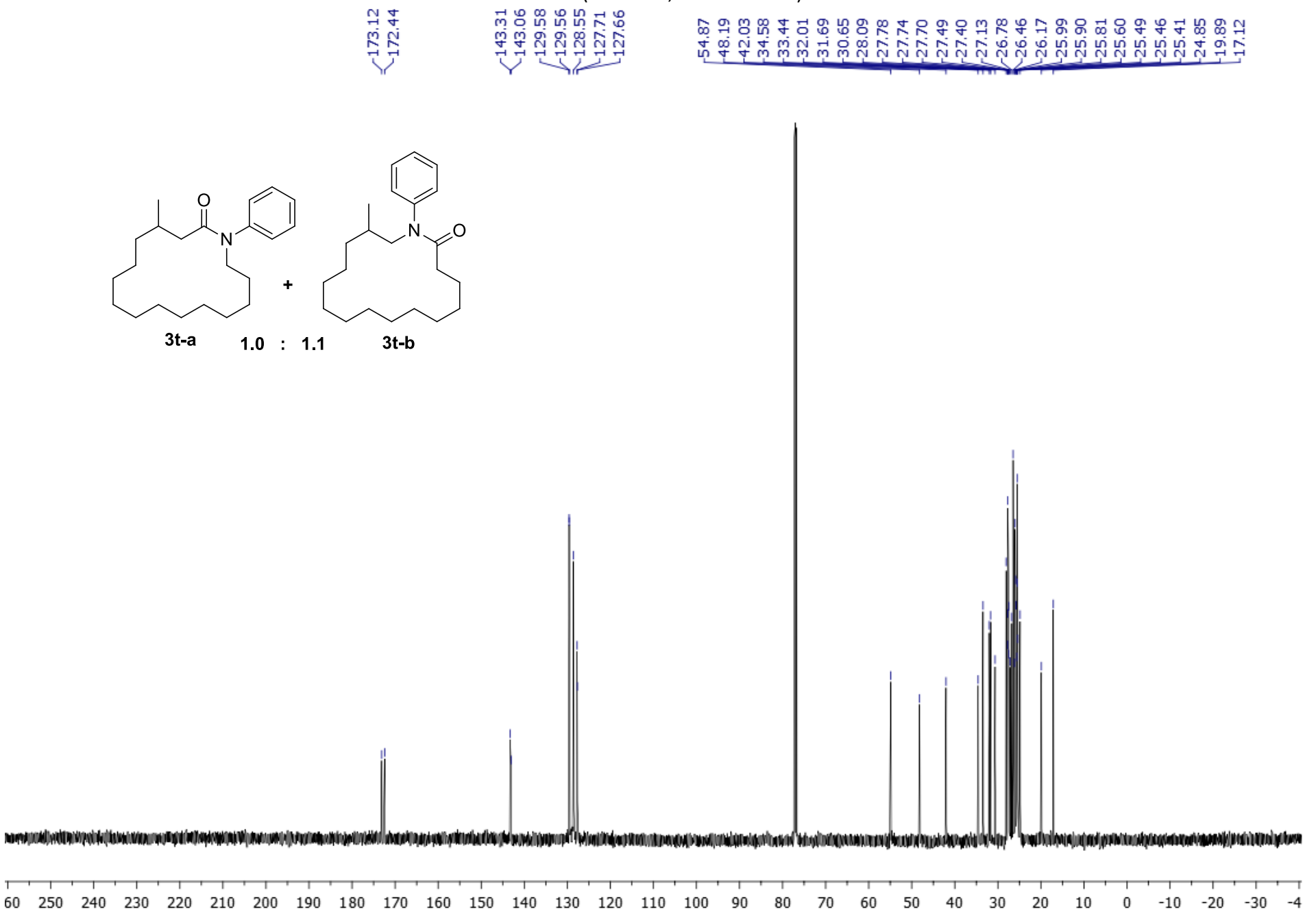
***p*-4r**

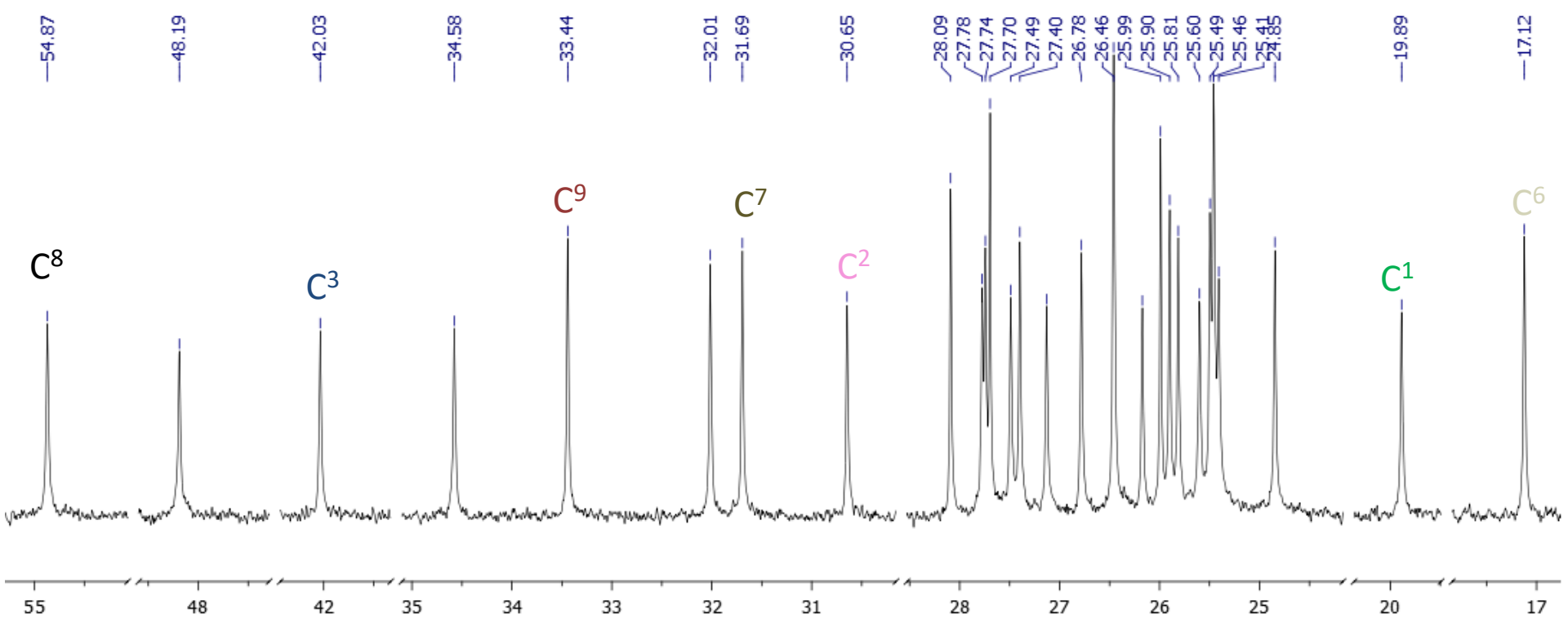
^{1}H NMR (600 MHz, chloroform-*d*)

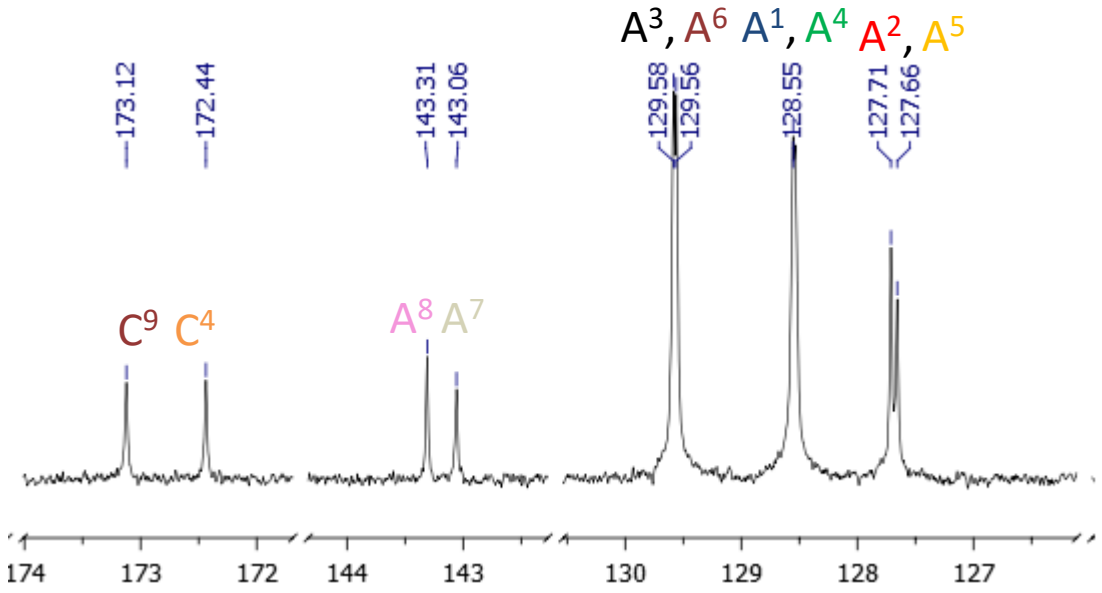


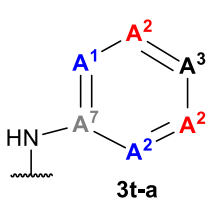

H1
H8
H2
H9
H12
H5
H11
H3
H4
H7
CH3
CH3
P2, P5
P3, P6
P1, P4
3t-a
3t-b
3t-a
3t-b

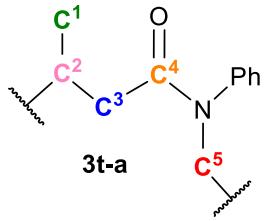
^{13}C NMR (151 MHz, chloroform-*d*)

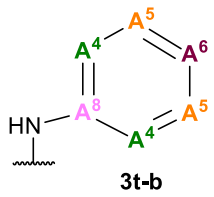


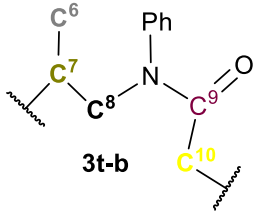

54.87
48.19
42.03
34.58
33.44
32.01
31.69
30.65
28.09
27.78
27.74
27.70
27.49
27.40
26.78
26.46
25.99
25.90
25.81
25.60
25.49
25.46
25.41
24.85
19.89
17.12
C8
C3
C9
C7
C2
C1
C6
55
48
42
35
34
33
32
31
28
27
26
25
20
17


A3, A6 A1, A4 A2, A5
173.12
172.44
143.31
143.06
129.58
129.56
128.55
127.71
127.66
C9 C4
A8 A7
174
173
172
144
143
130
129
128
127

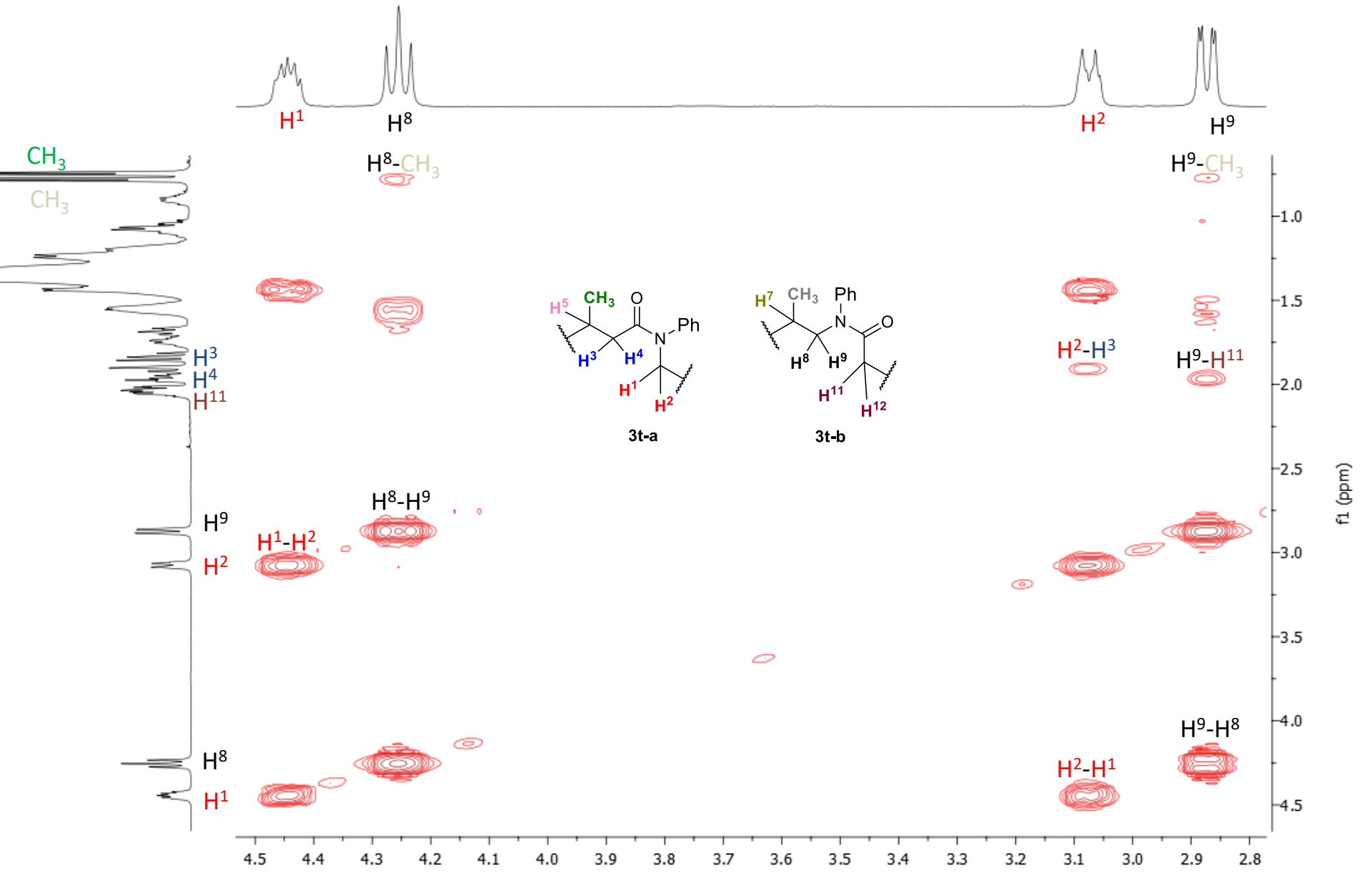

A2
A1
A3
HN
A7
A2
A2
3t-a

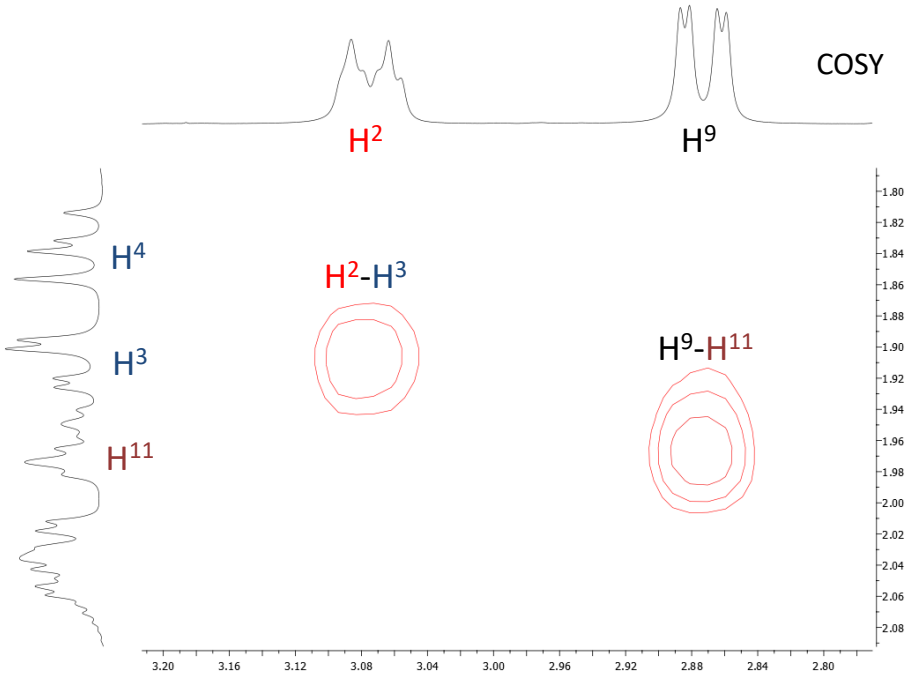

C1
O
C2
C4
C3
Ph
N
3t-a
C5

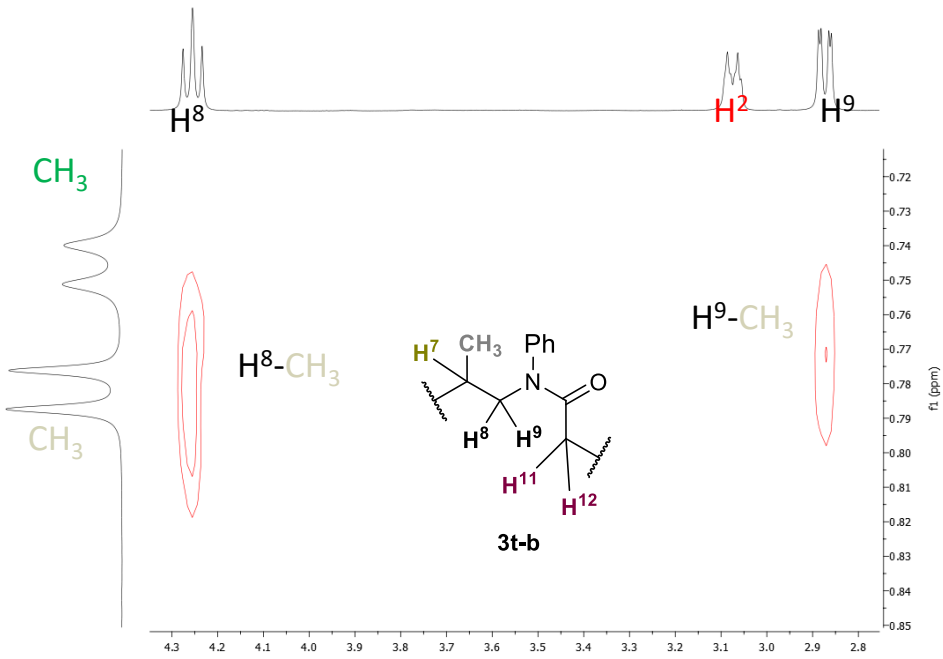

A5
A4
A6
HN
A8
A5
A4
3t-b

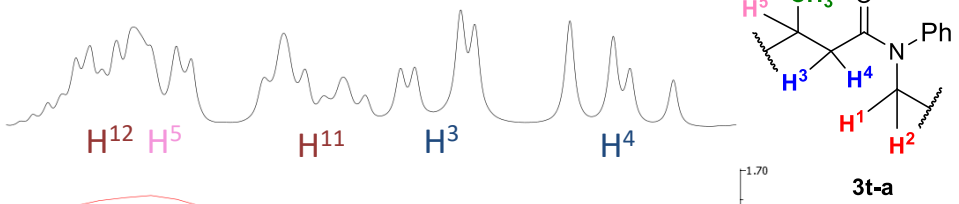

C6
Ph
C7
N
O
C8
C9
3t-b
C10

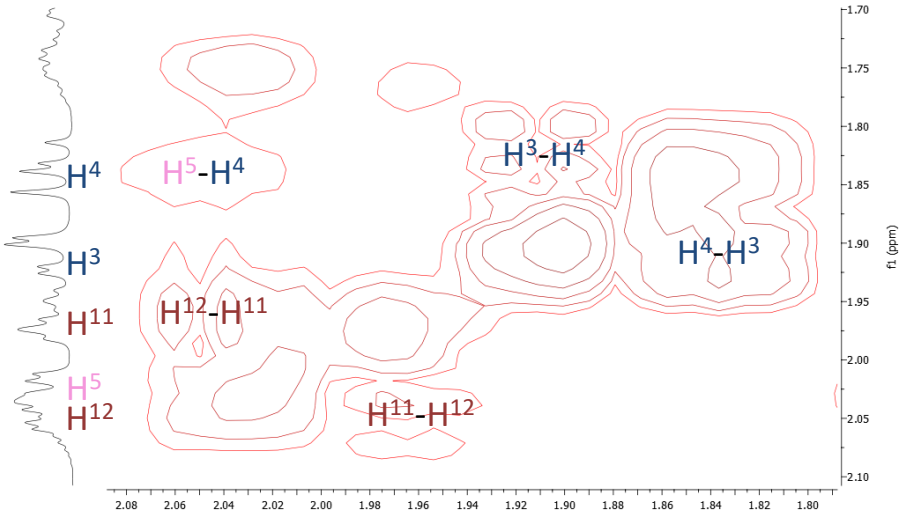
COSY

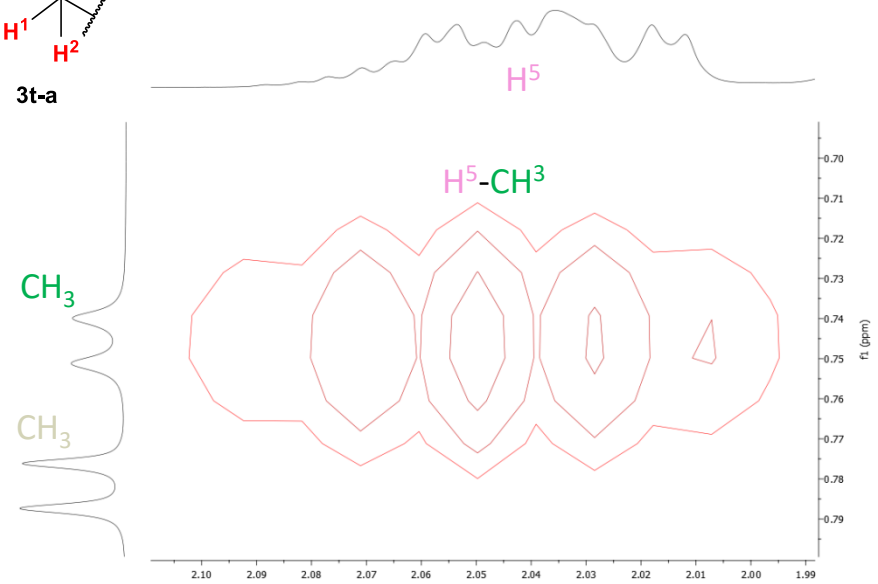

H1
H8
H2
H9
CH3
CH3
H8-CH3
H9-CH3
H3
H4
H11
H2-H3
H9-H11
H8-H9
H1-H2
H9
H2
H8
H1
H9-H8
H2-H1
3t-a
3t-b
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
f1 (ppm)


COSY
H2
H9
H4
H3
H11
H2-H3
H9-H11

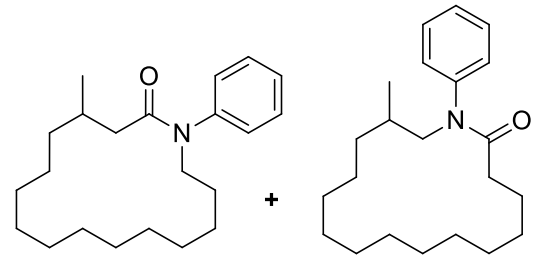

H8
H2
H9
CH3
CH3
H8-CH3
H9-CH3
H7
CH3
Ph
N
O
H8
H9
H11
H12
3t-b


H5
CH3
O
Ph
N
H3
H4
H1
H2
3t-a

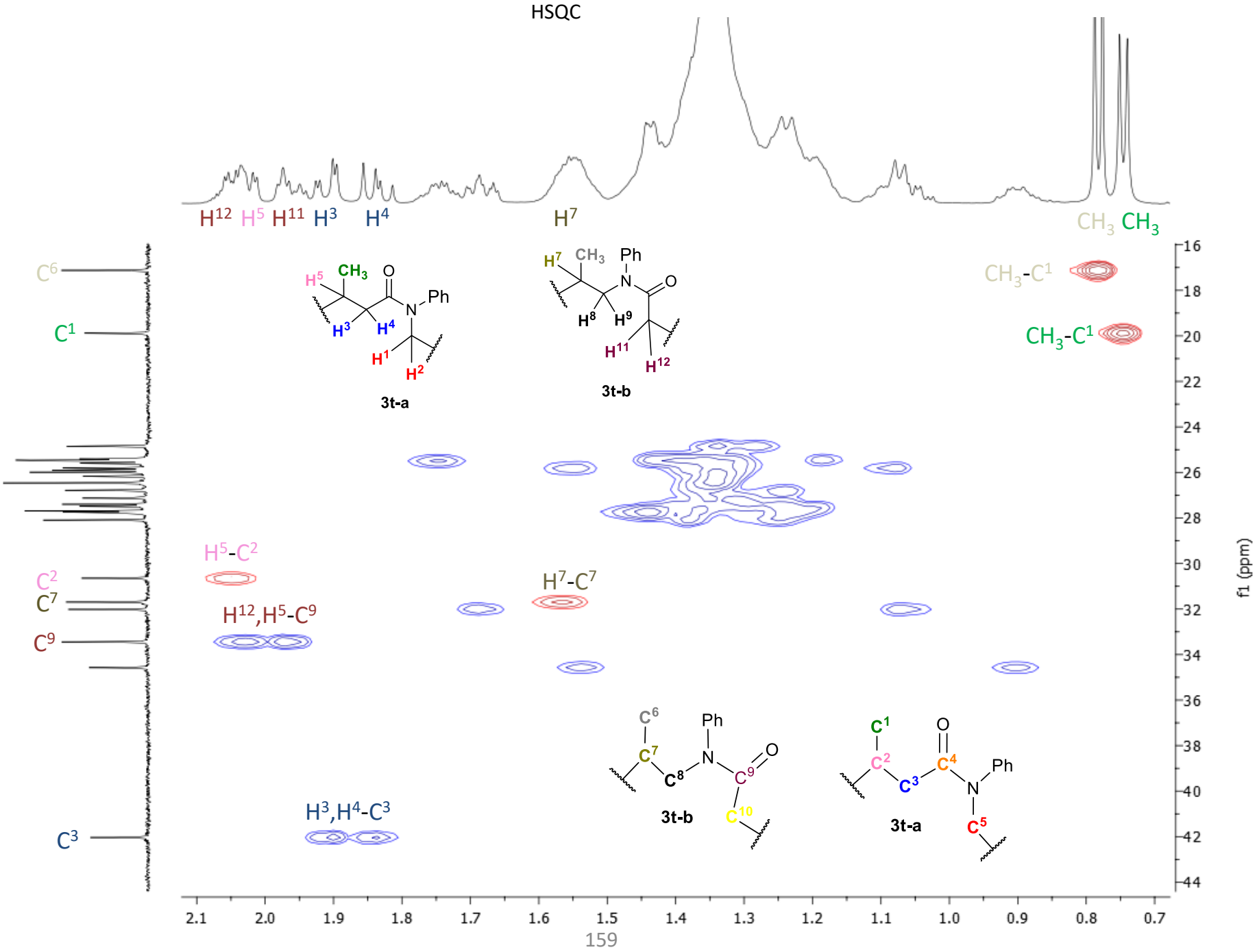

H12
H5
H11
H3
H4
H4
H5-H4
H3-H4
H4-H3
H3
H11
H12-H11
H5
H12
H11-H12


H5
H5-CH3
CH3
CH3

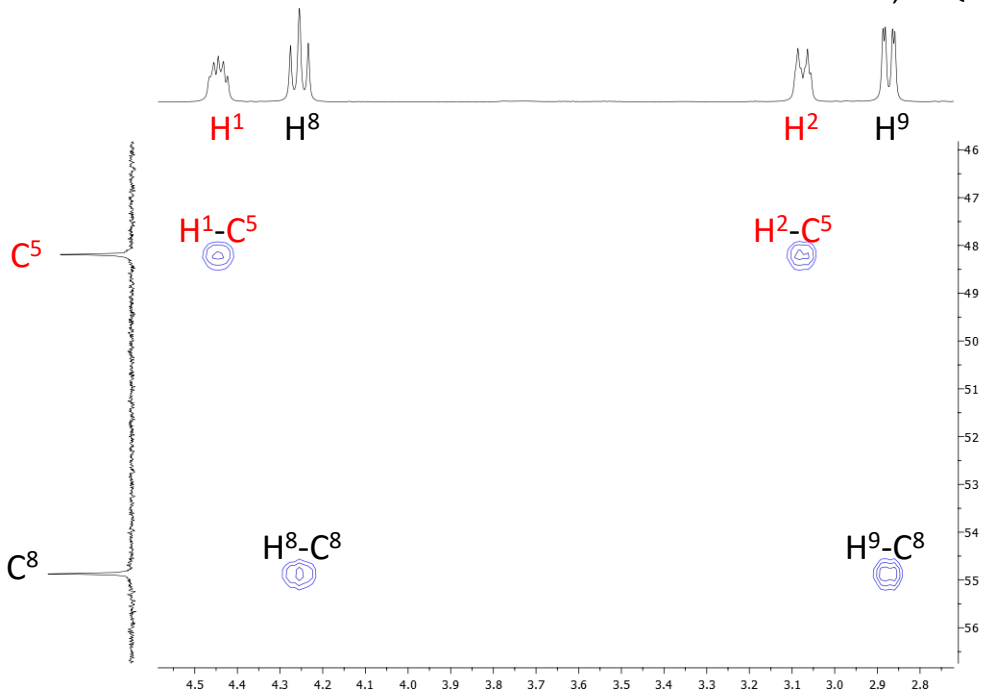
HSQC

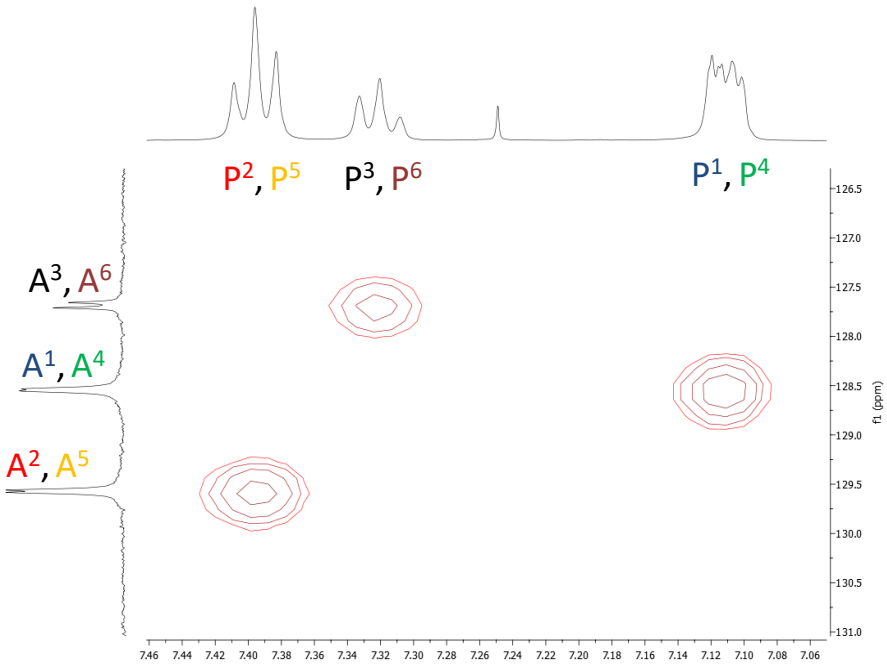


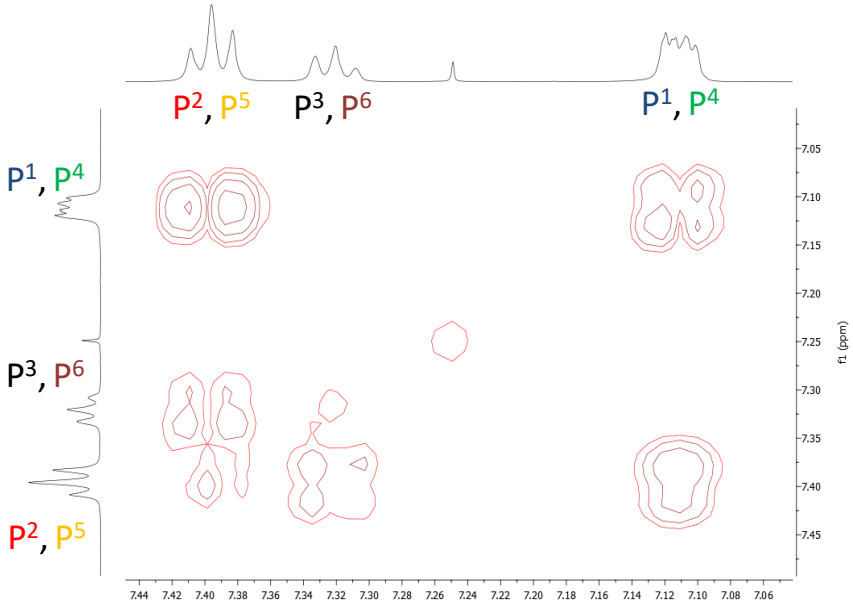
3t-a 1.0 : 1.1 3t-b

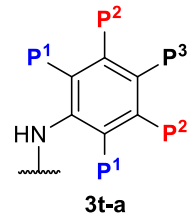

HSQC
H12 H5 H11 H3 H4
H7
CH3 CH3
C6
C1
C2
C7
C9
C3
H5-C2
H12,H5-C9
H7-C7
H3,H4-C3
CH3-C1
CH3-C1
3t-a
3t-b
3t-b
3t-a
2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7
16 18 20 22 24 26 28 30 32 34 36 38 40 42 44
f1 (ppm)

COSY, HSQC

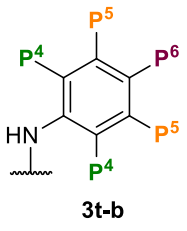




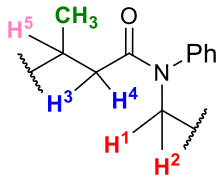




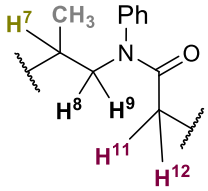
3t-a



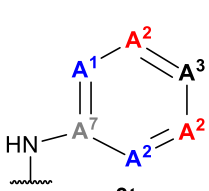
3t-b



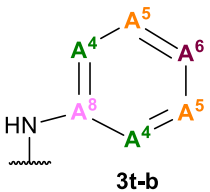
3t-a



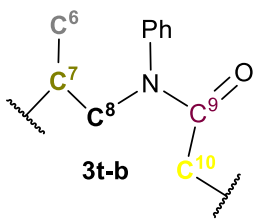
3t-b



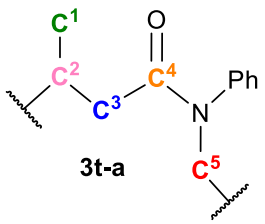
3t-a



3t-b

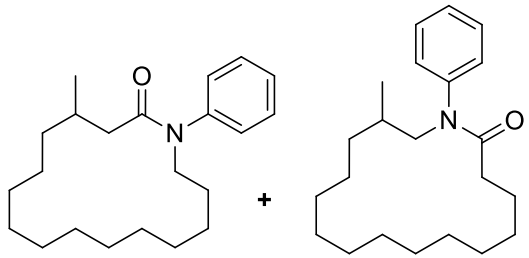


3t-b

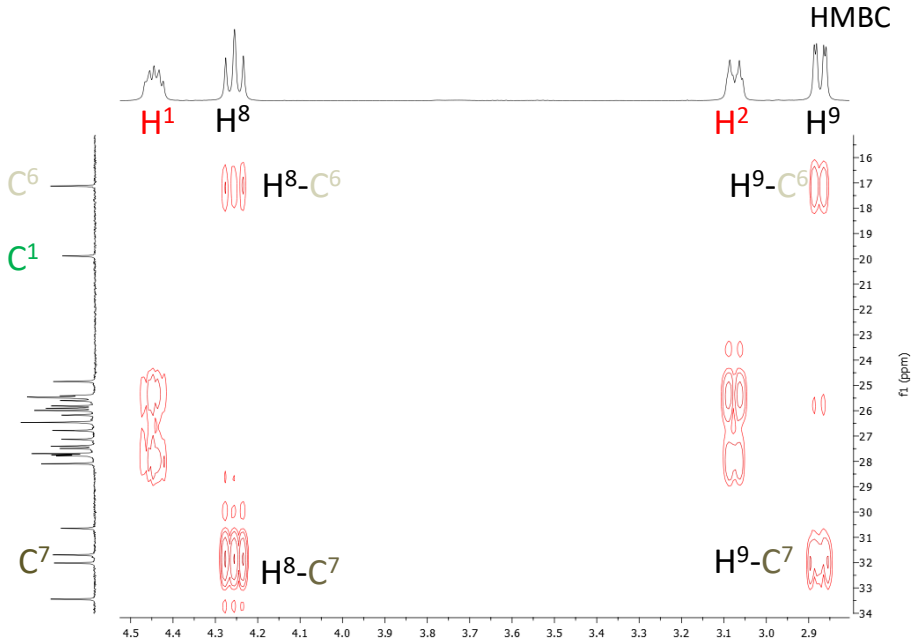


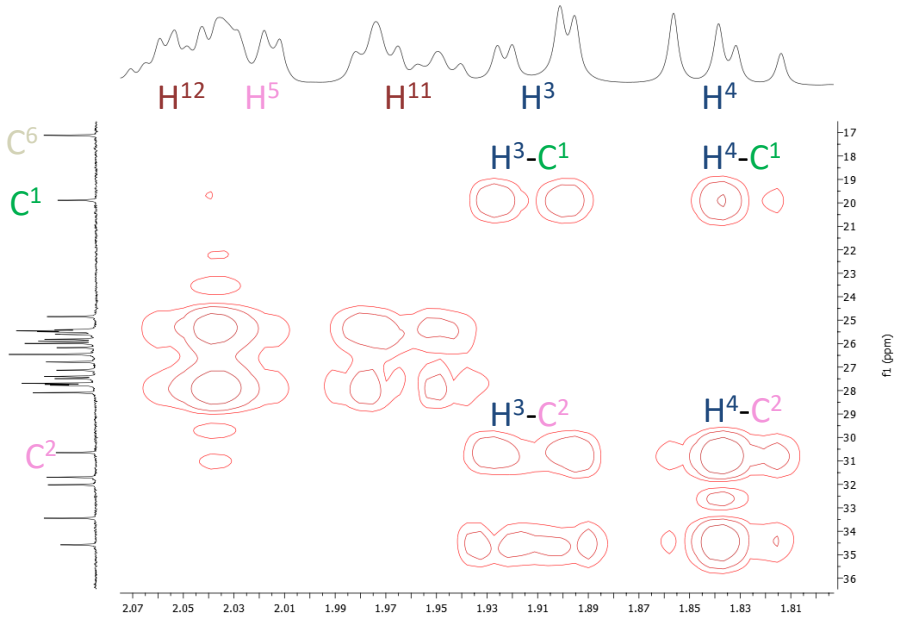
3t-a

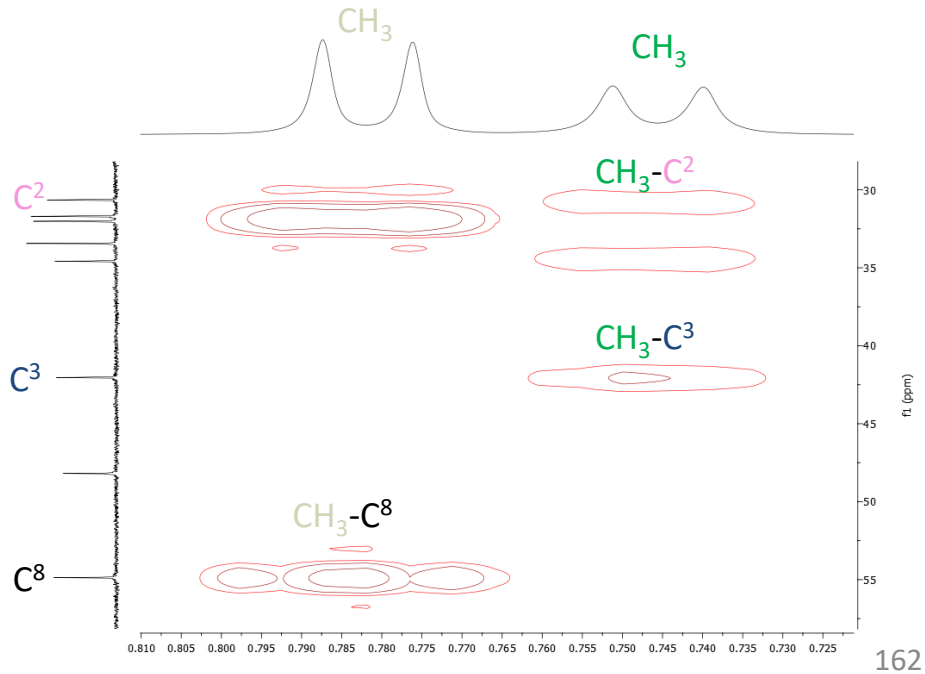
HMBC

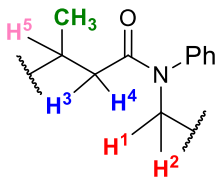


3t-a 1.0 : 1.1 3t-b

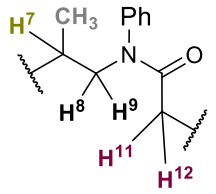




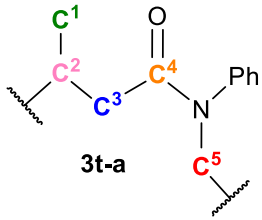




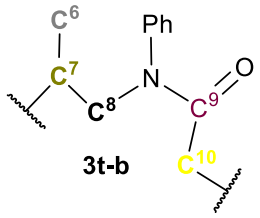
3t-a



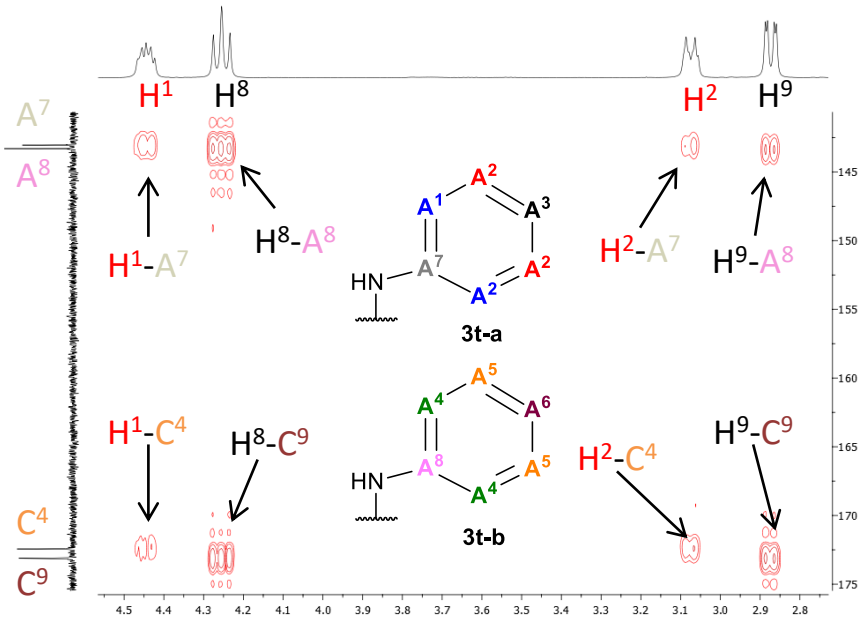
3t-b

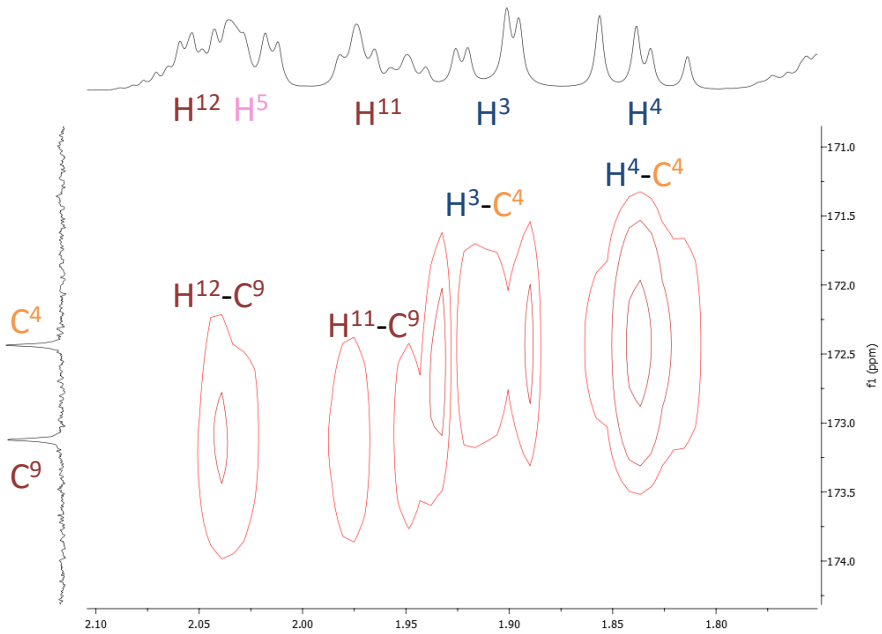


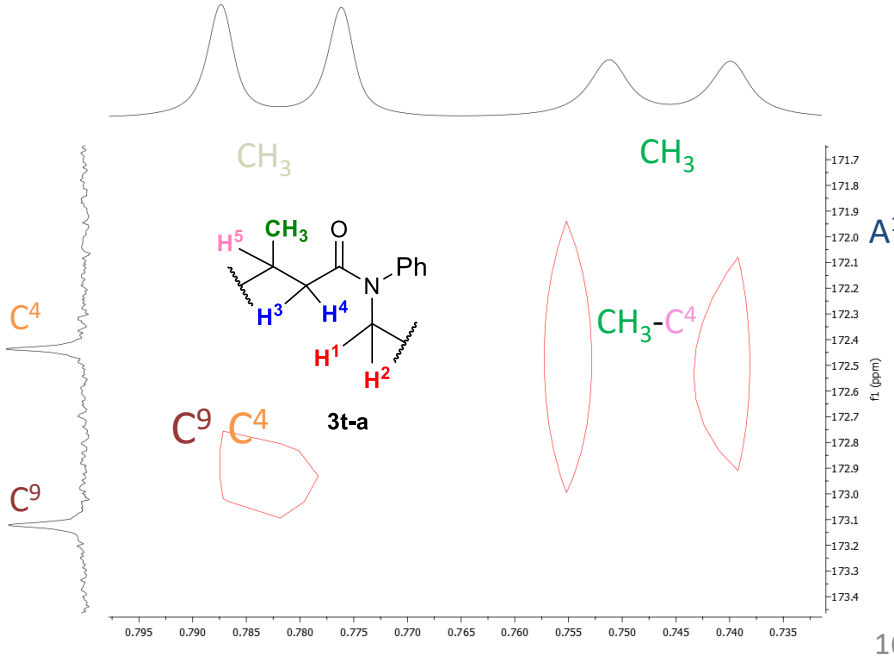
3t-a

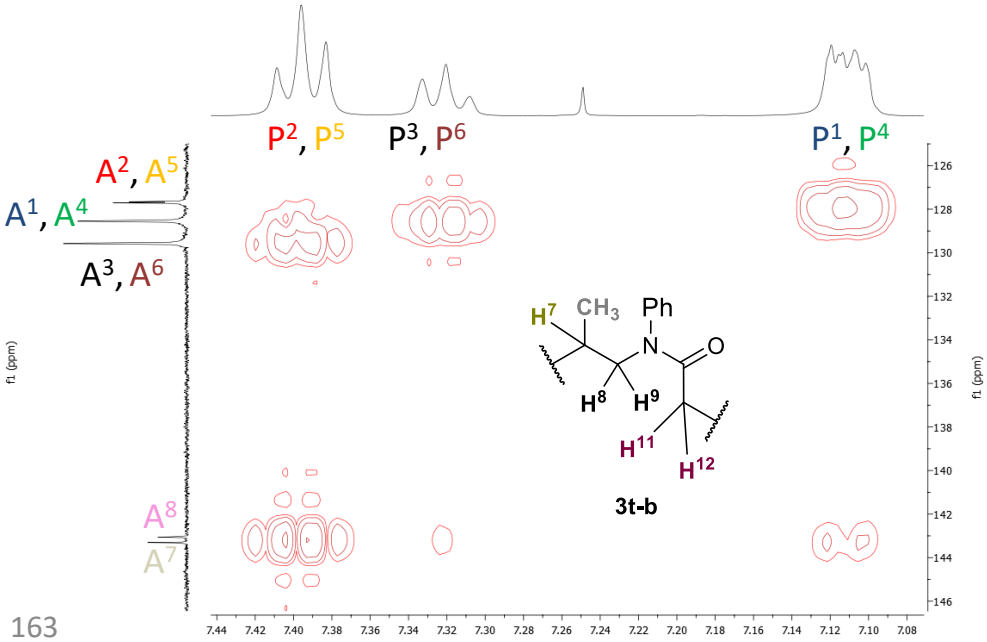


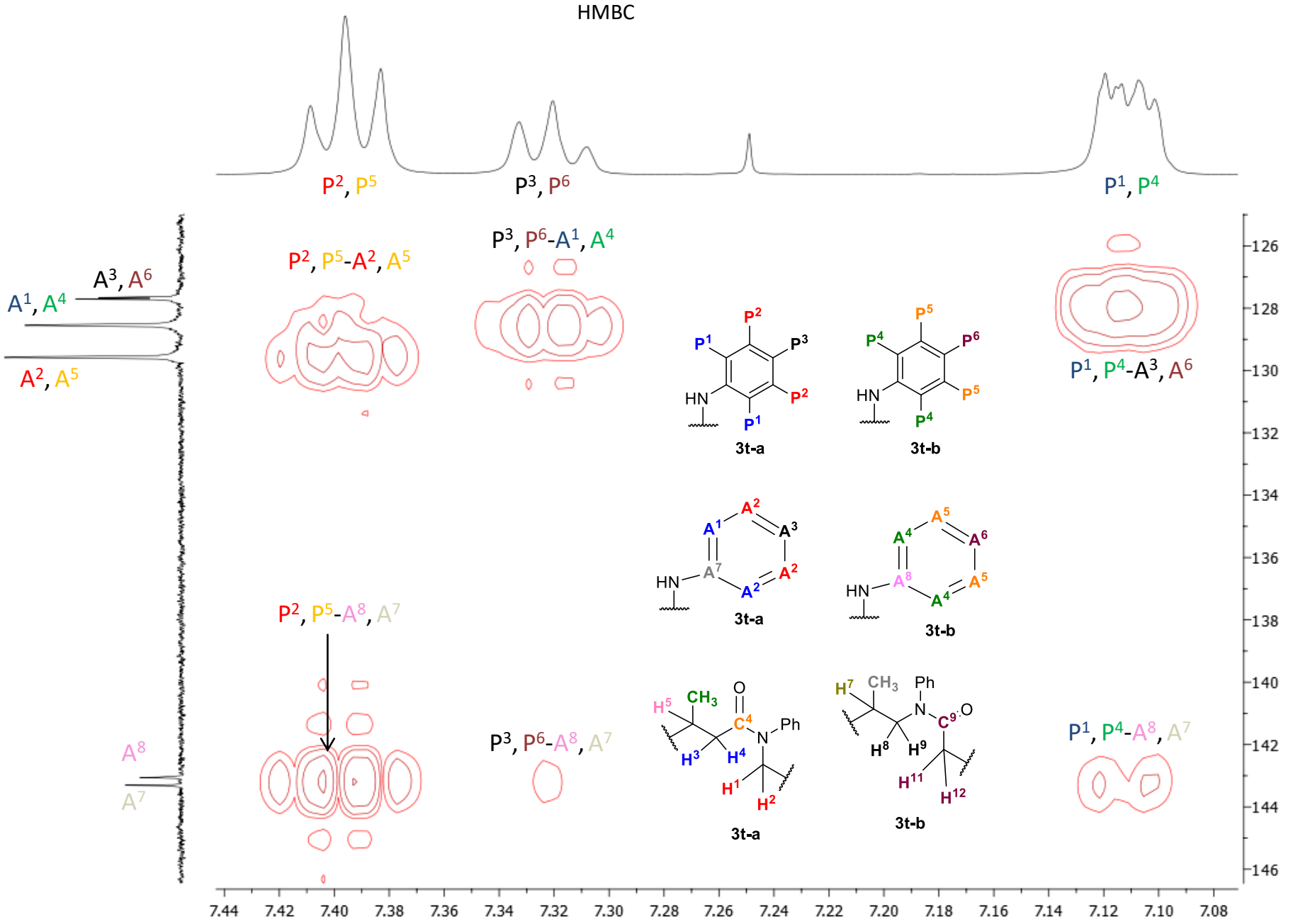
3t-b


H1
H8
H2
H9
A7
A8
H1-A7
H8-A8
H2-A7
H9-A8
HN
3t-a
H1-C4
H8-C9
H2-C4
H9-C9
C4
C9
3t-b

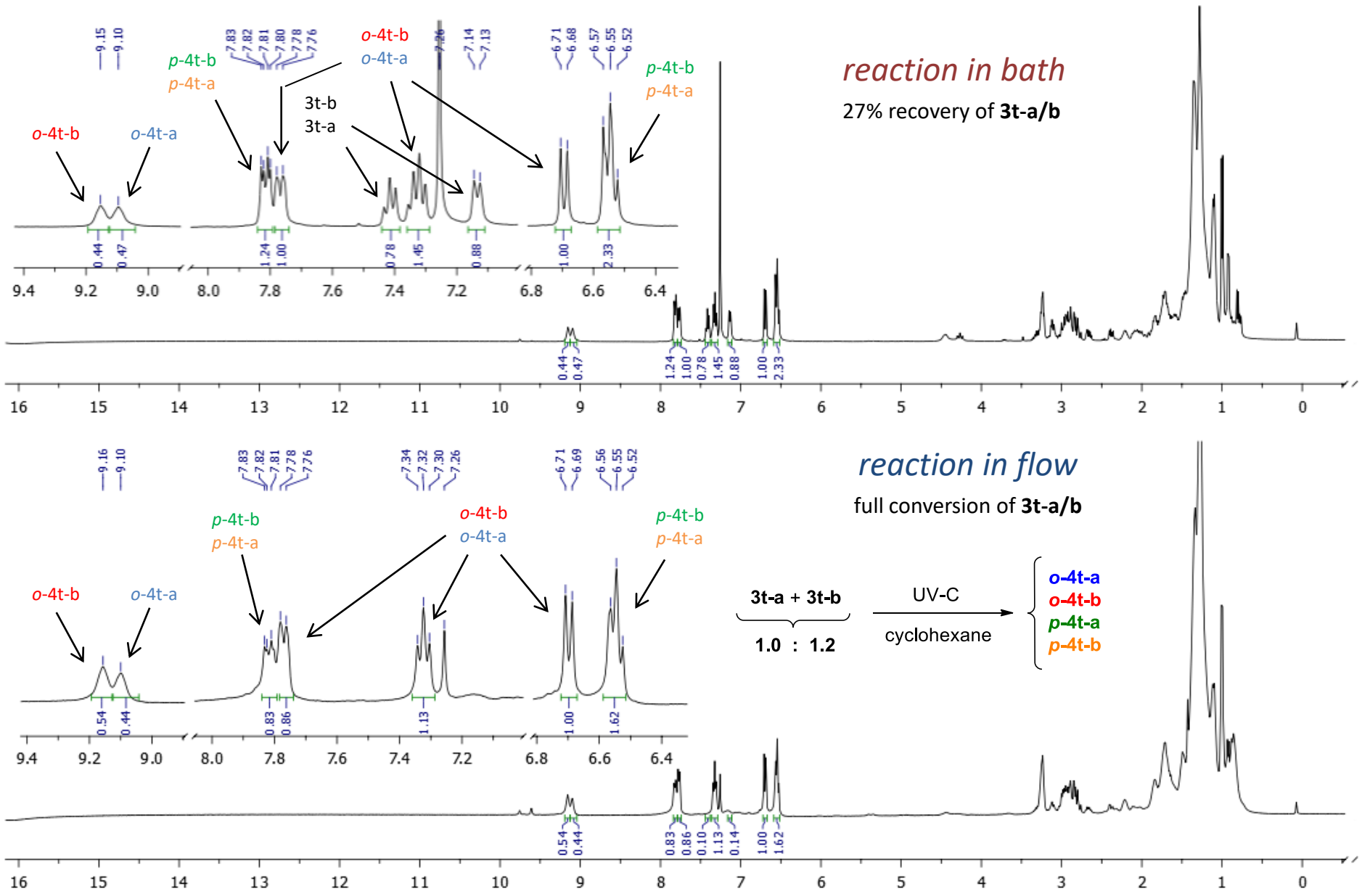

H12 H5
H11
H3
H4
H4-C4
H3-C4
H12-C9
H11-C9
C4
C9


CH3
CH3
H5
CH3
O
Ph
H3
H4
H1
H2
3t-a
C9 C4
CH3-C4
C4
C9

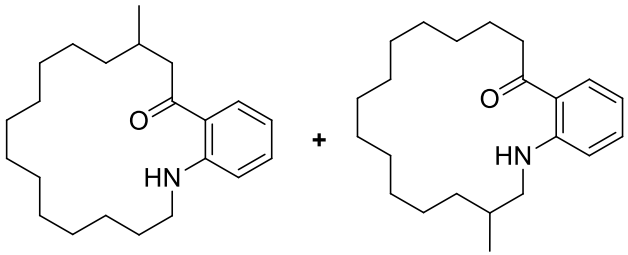

A2, A5
A1, A4
A3, A6
P2, P5
P3, P6
P1, P4
H7
CH3
Ph
N
O
H8
H9
H11
H12
3t-b
A8
A7


HMBC
P2, P5
P3, P6
P1, P4
A3, A6
A1, A4
A2, A5
A8
A7
P2, P5-A2, A5
P3, P6-A1, A4
P1, P4-A3, A6
P2, P5-A8, A7
P3, P6-A8, A7
P1, P4-A8, A7
3t-a
3t-b
3t-a
3t-b
3t-a
3t-b
7.44
7.42
7.40
7.38
7.36
7.34
7.32
7.30
7.28
7.26
7.24
7.22
7.20
7.18
7.16
7.14
7.12
7.10
7.08
126
128
130
132
134
136
138
140
142
144
146
f1 (ppm)

^{1}H NMR (400 MHz, Chloroform-*d*) of crude reaction mixture

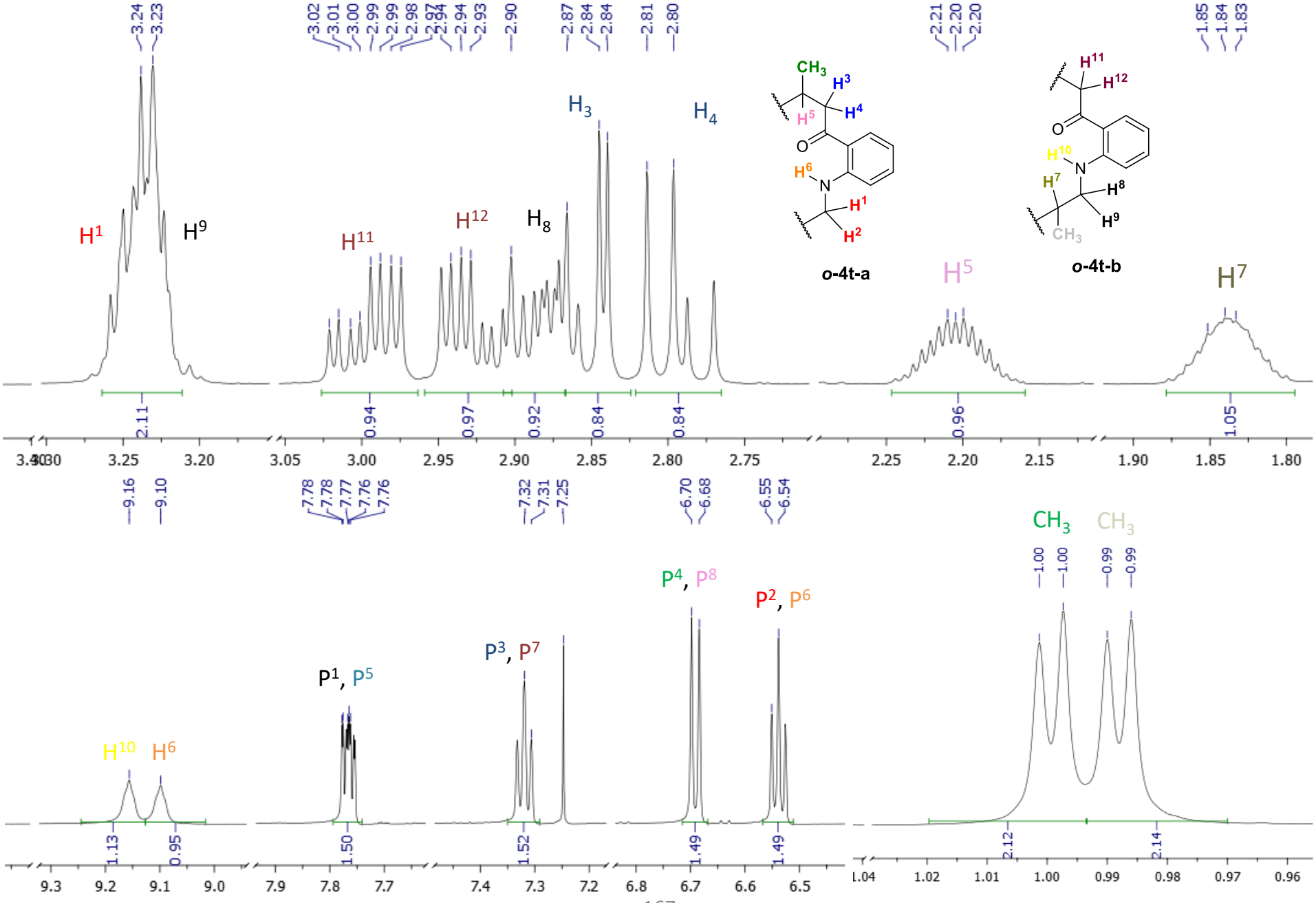


^{1}H NMR (600 MHz, chloroform-*d*)

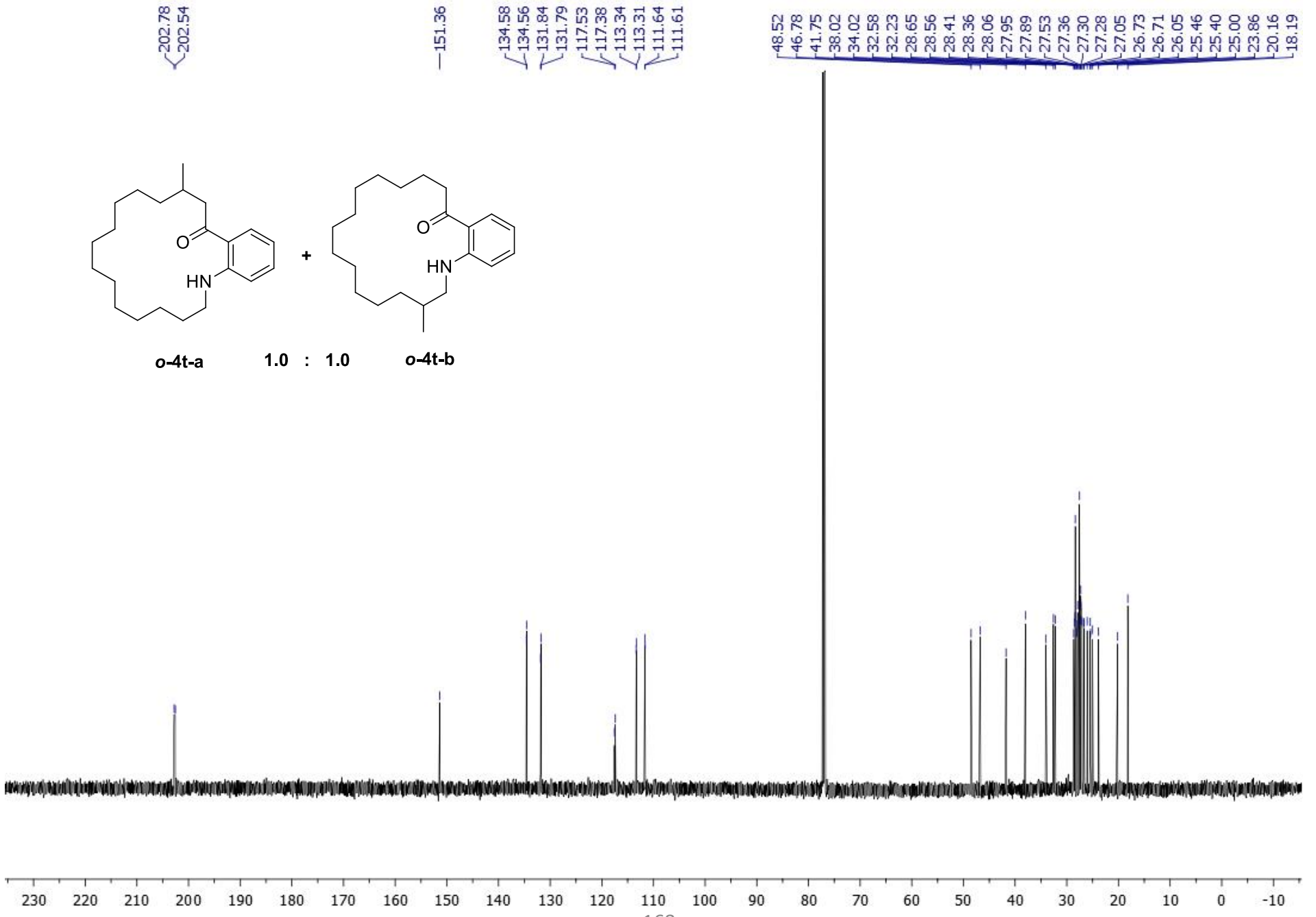


***o*-4t-a** **1.0 : 1.0** ***o*-4t-b**

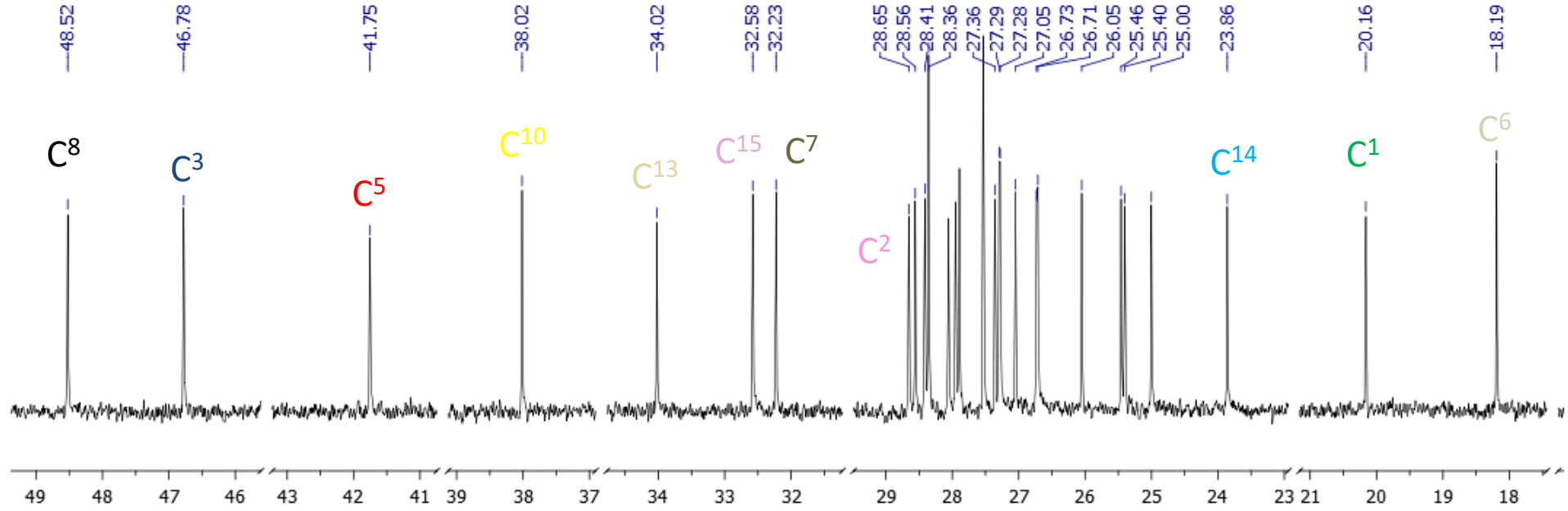
^{1}H NMR (600 MHz, chloroform-*d*)

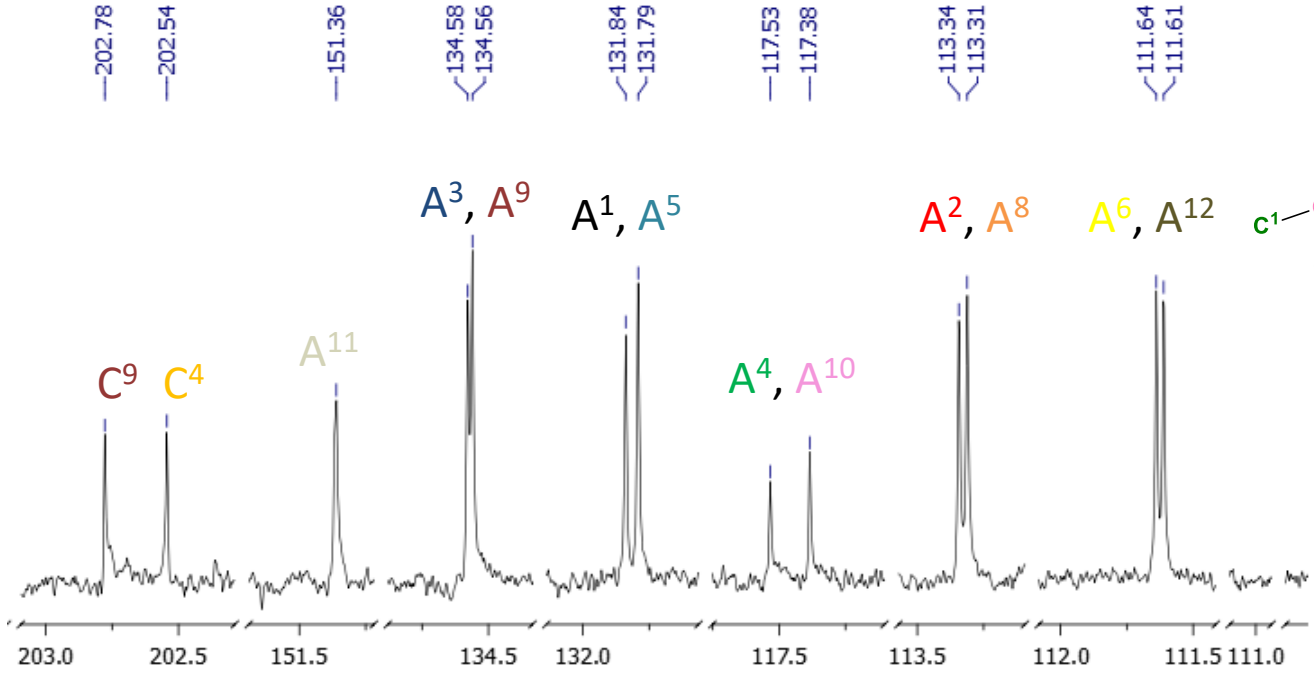


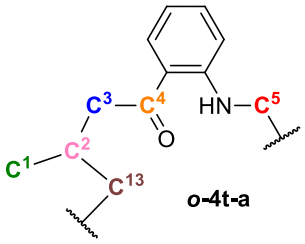
^{13}C NMR (151 MHz, chloroform-*d*)

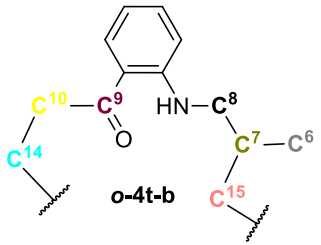


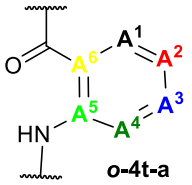
^{13}C NMR (151 MHz, chloroform-*d*)

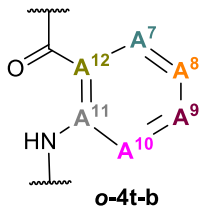




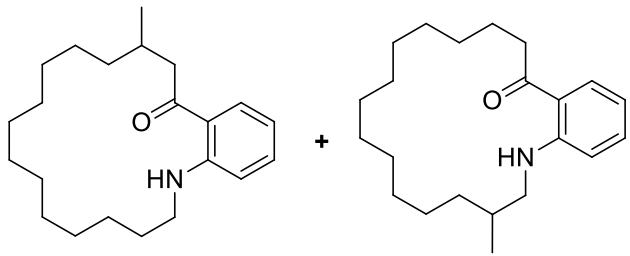








COSY

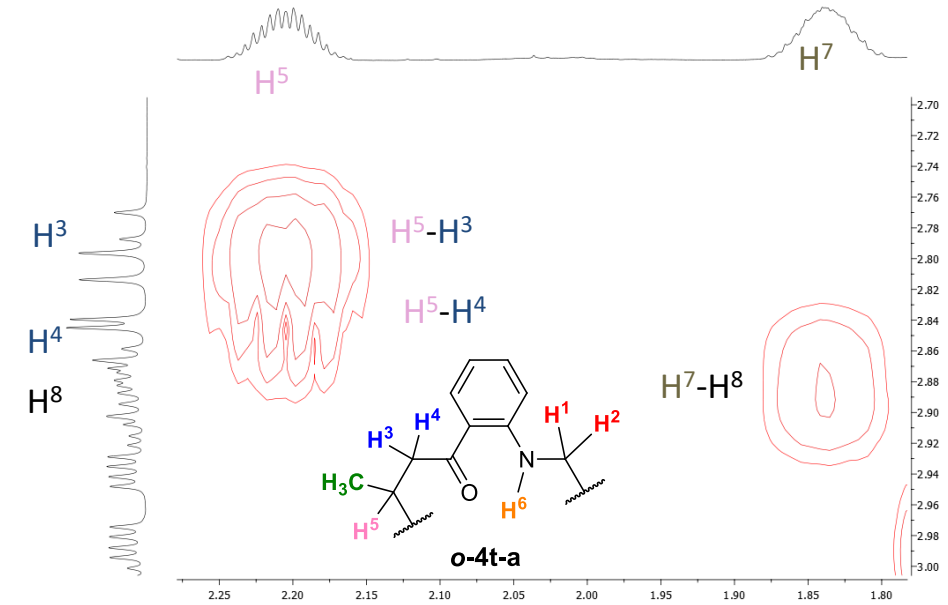


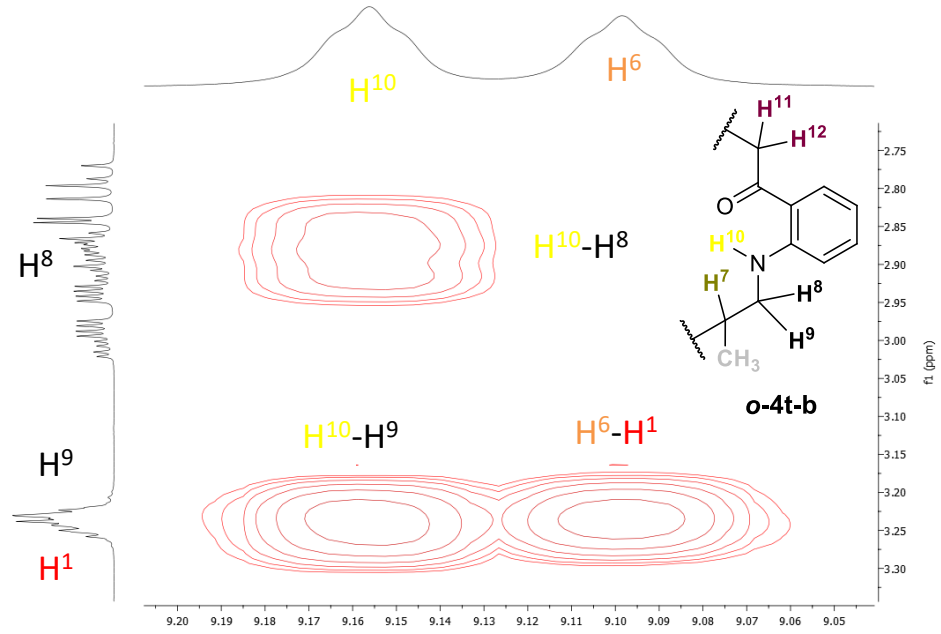
+

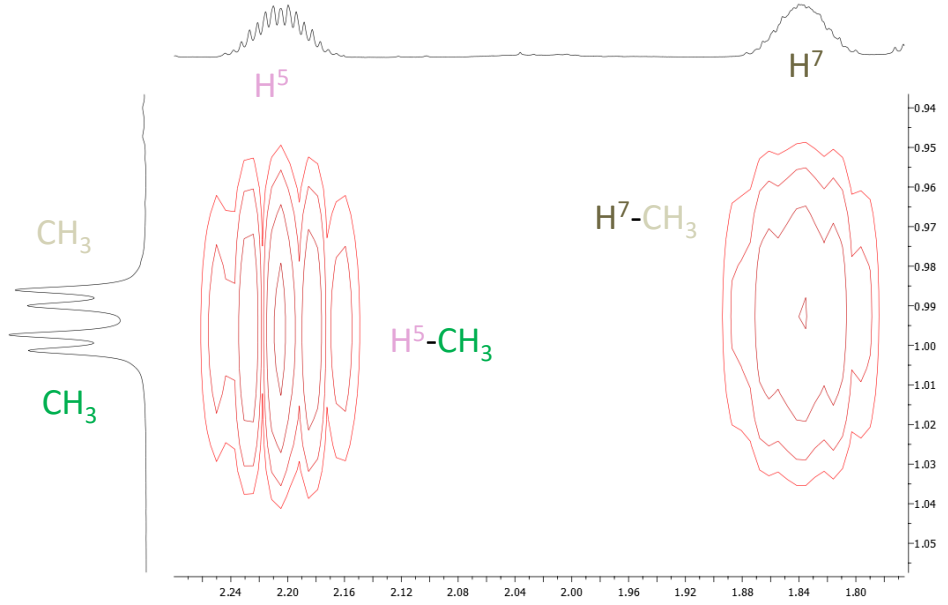
***o*-4t-a** **1.0 : 1.0** ***o*-4t-b**

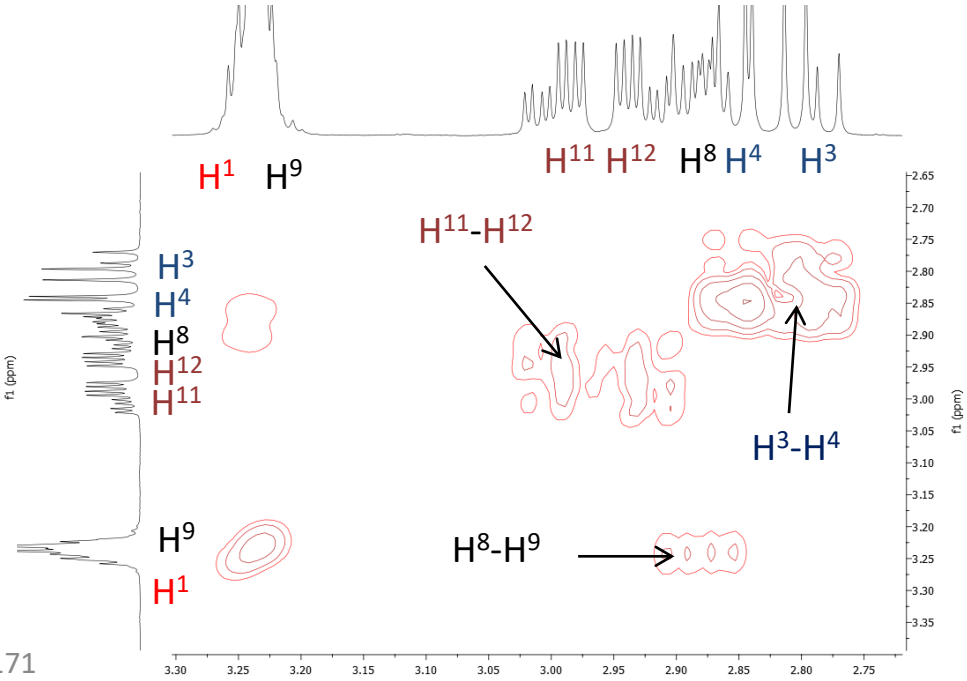
f1 (ppm)

COSY

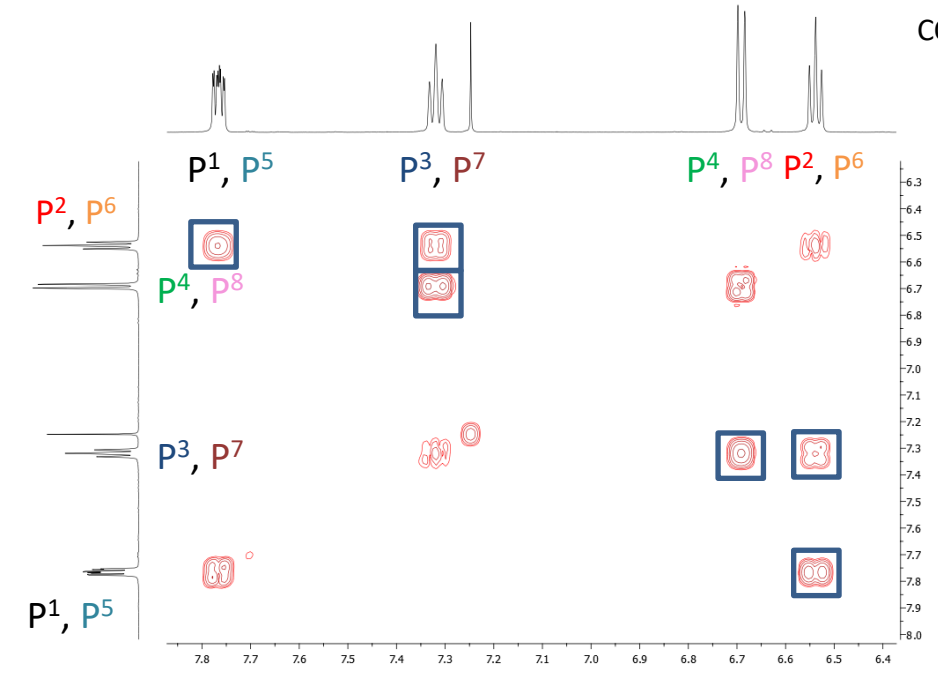

H5
H7
H3
H4
H8
H5-H3
H5-H4
H7-H8
o-4t-a

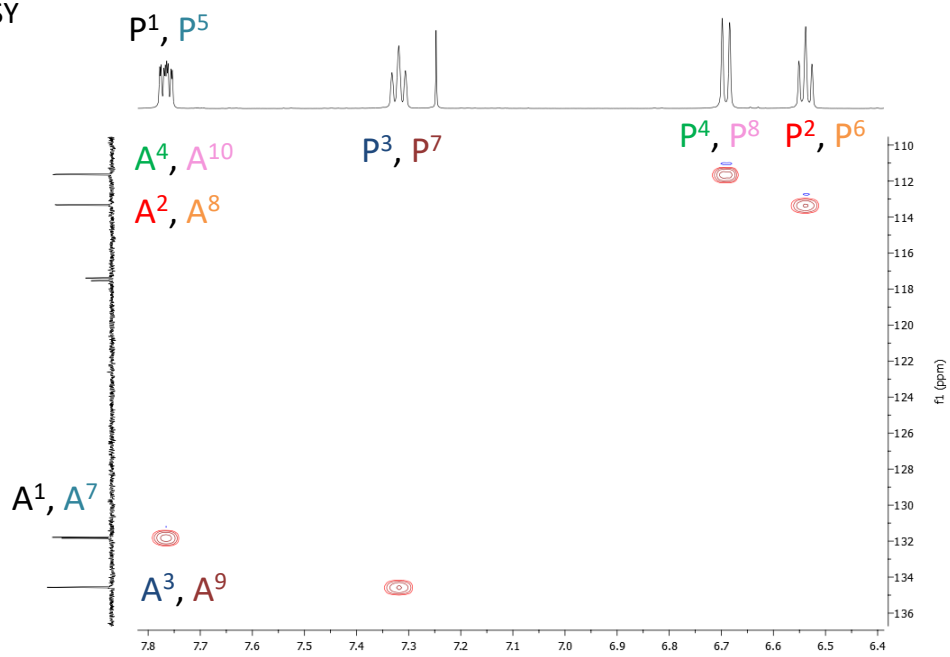

H10
H6
H8
H9
H1
H10-H8
H10-H9
H6-H1
o-4t-b

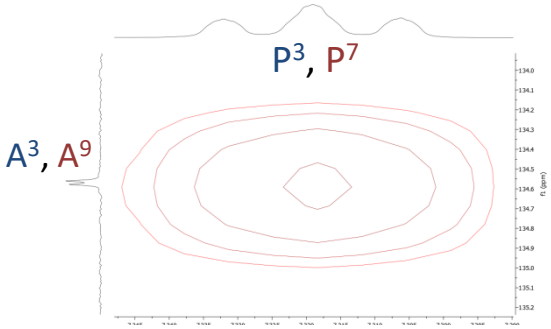

H5
H7
CH3
CH3
H5-CH3
H7-CH3

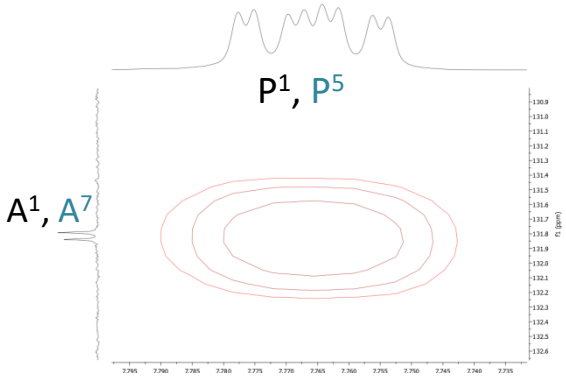

H1
H9
H11
H12
H8
H4
H3
H3
H4
H8
H12
H11
H11-H12
H3-H4
H9
H1
H8-H9

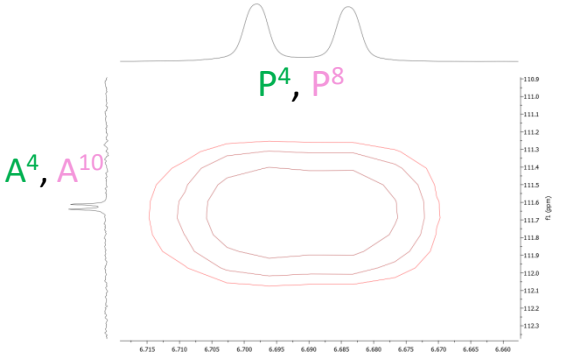
COSY

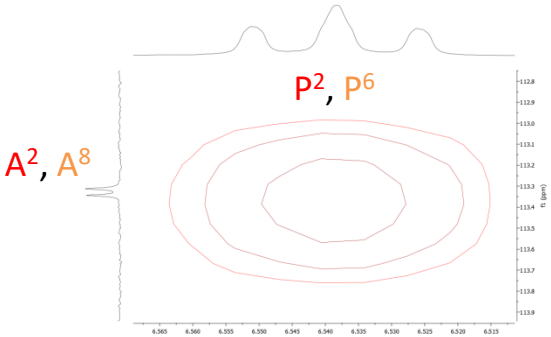


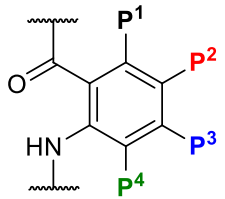




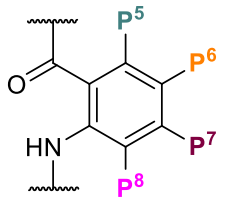




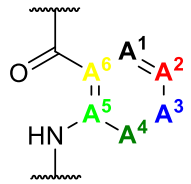




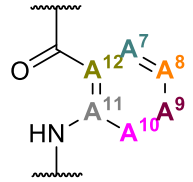
o-4t-a



o-4t-b

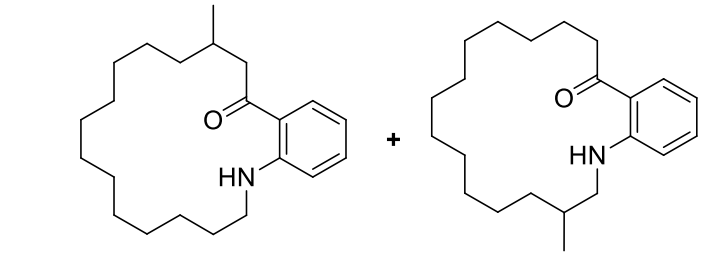


o-4t-a



o-4t-b

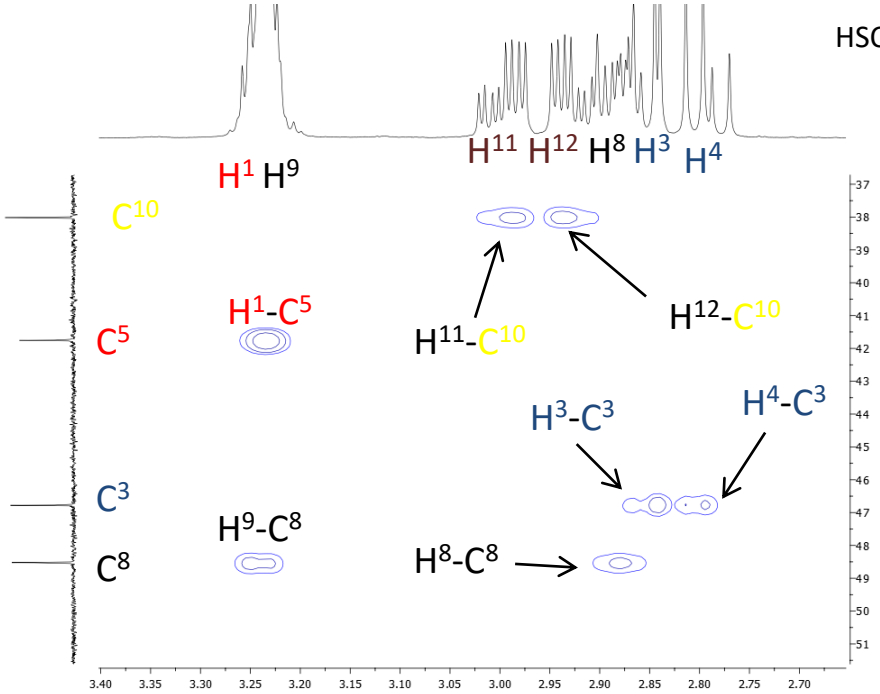
HSQC

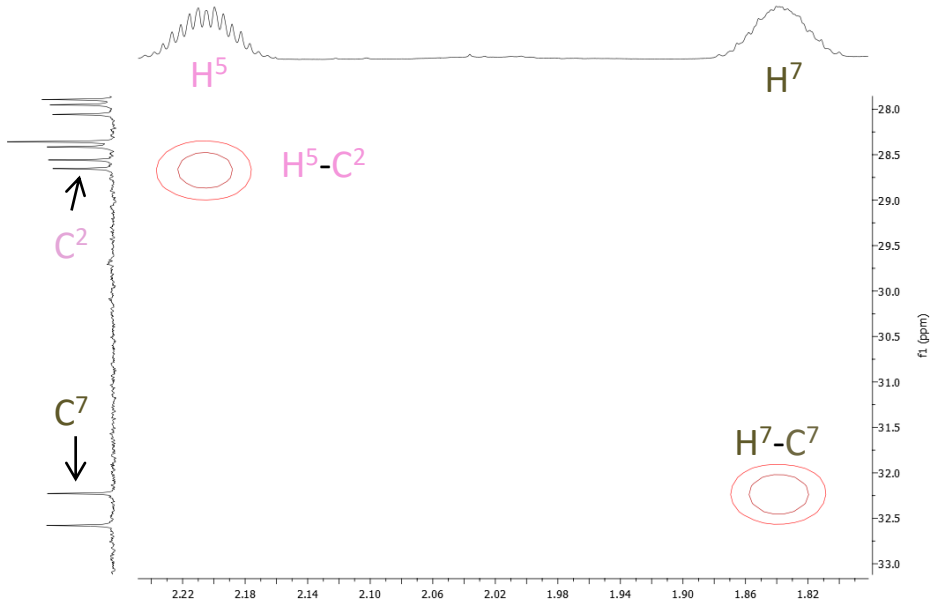


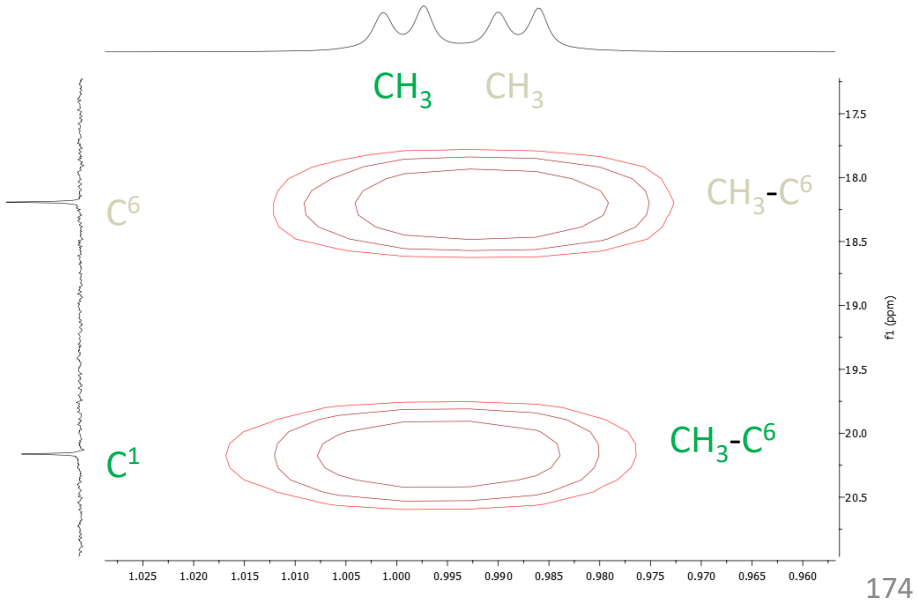
+

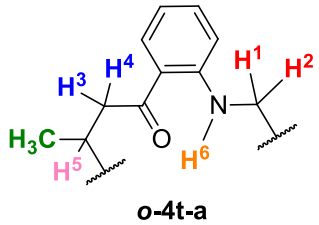
***o*-4t-a** **1.0 : 1.0** ***o*-4t-b**

HSQC

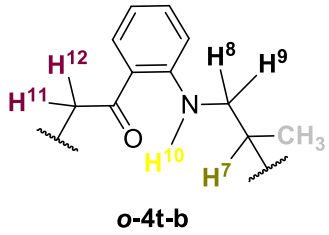




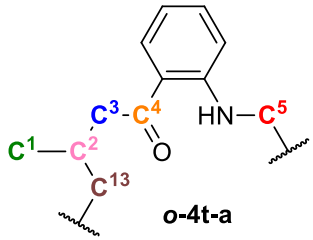




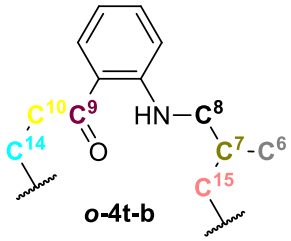
o-4t-a



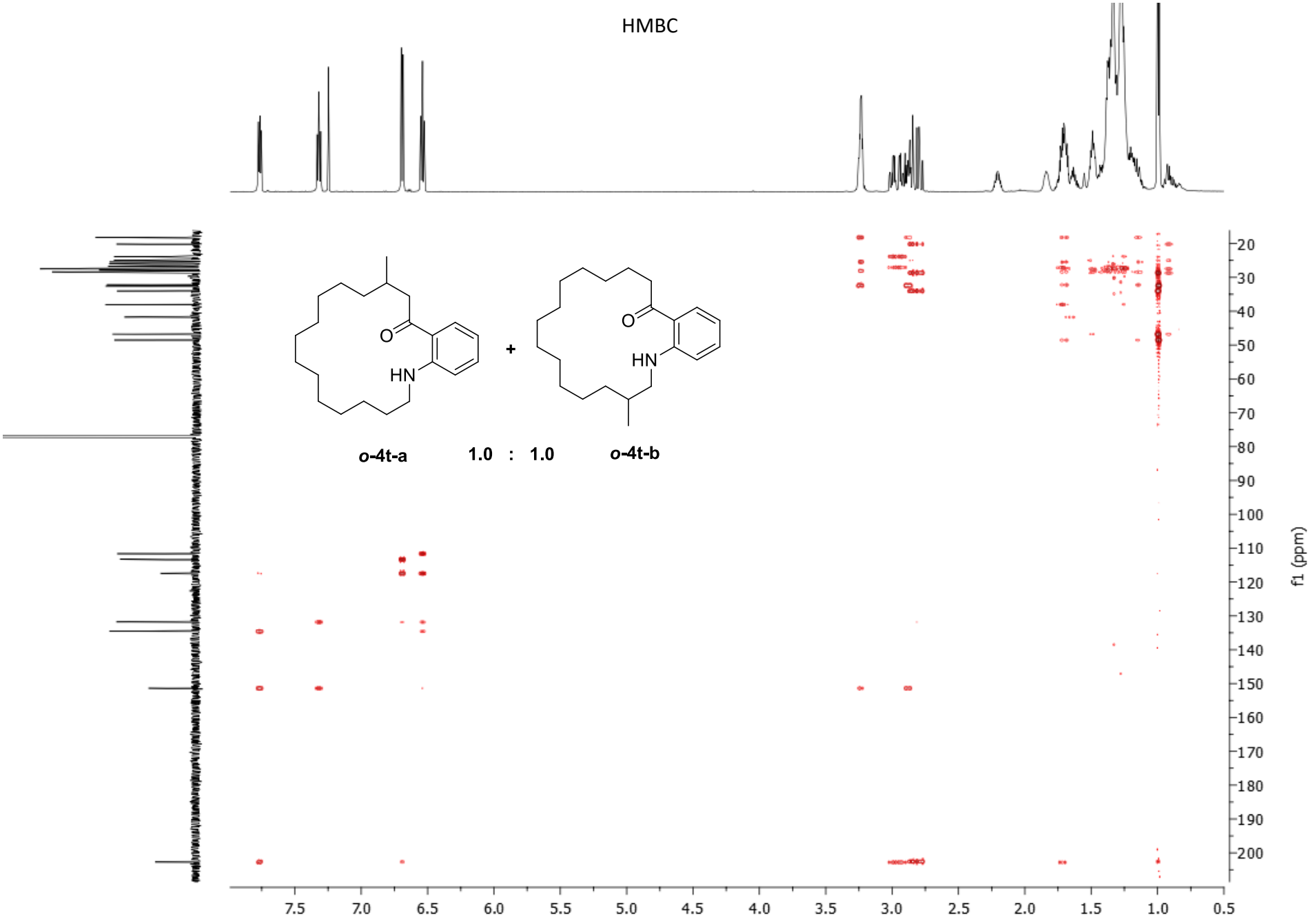
o-4t-b

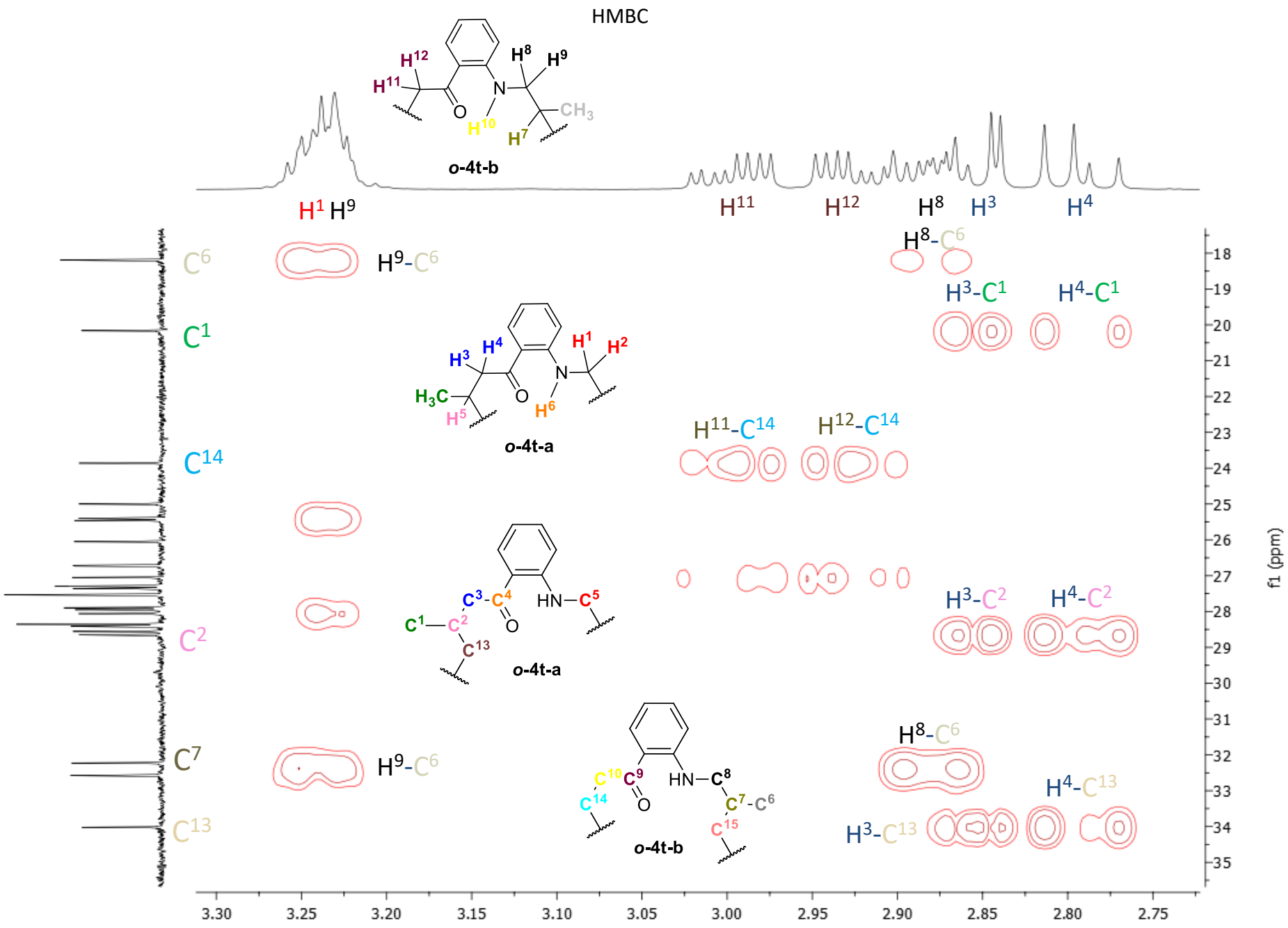


o-4t-a

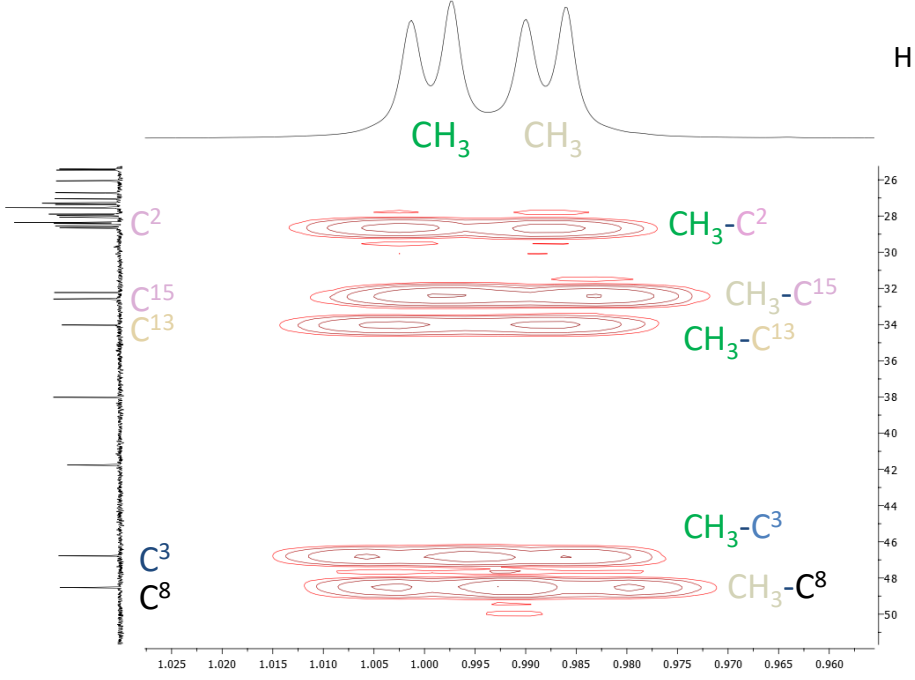


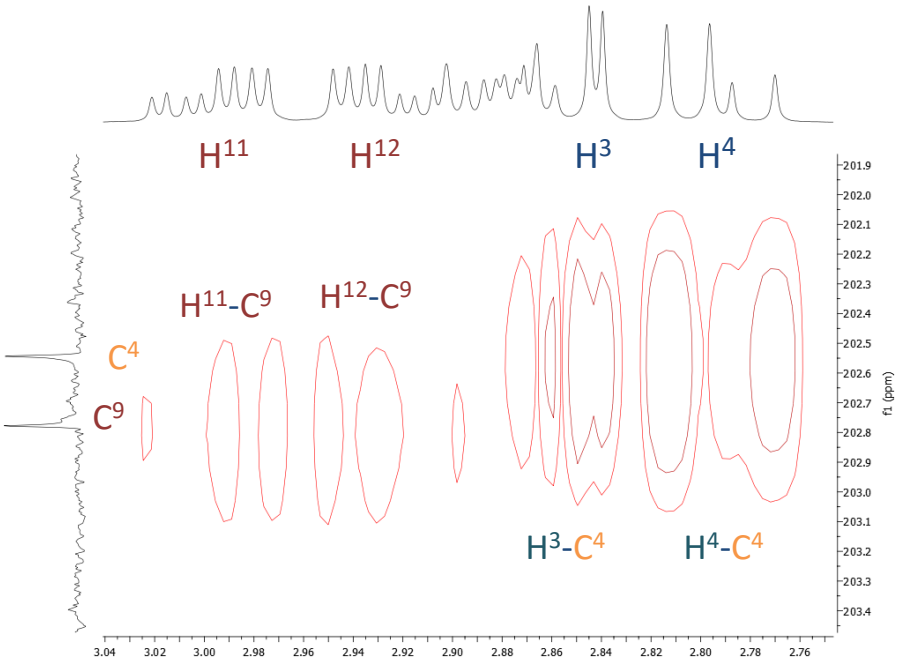
o-4t-b

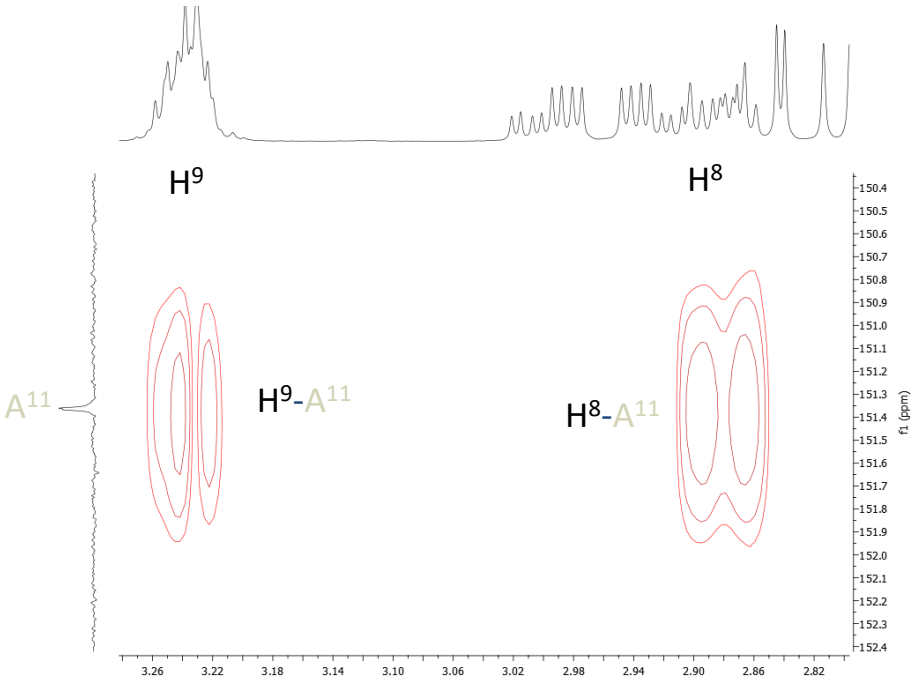

HMBC
O
HN
+
O
HN
o-4t-a
1.0 : 1.0
o-4t-b
f1 (ppm)

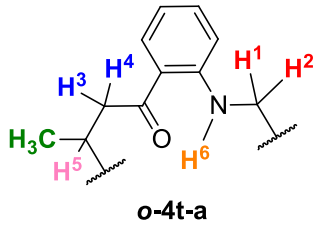

HMBC
o-4t-b
o-4t-a
o-4t-a
o-4t-b
H1 H9
H11
H12
H8
H3
H4
C6
C1
C14
C2
C7
C13
H9-C6
H8-C6
H3-C1
H4-C1
H11-C14
H12-C14
H3-C2
H4-C2
H9-C6
H8-C6
H4-C13
H3-C13
3.30
3.25
3.20
3.15
3.10
3.05
3.00
2.95
2.90
2.85
2.80
2.75
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
f1 (ppm)

HMBC

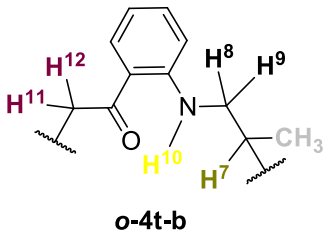




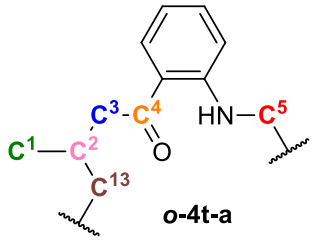




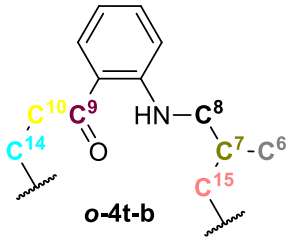
o-4t-a



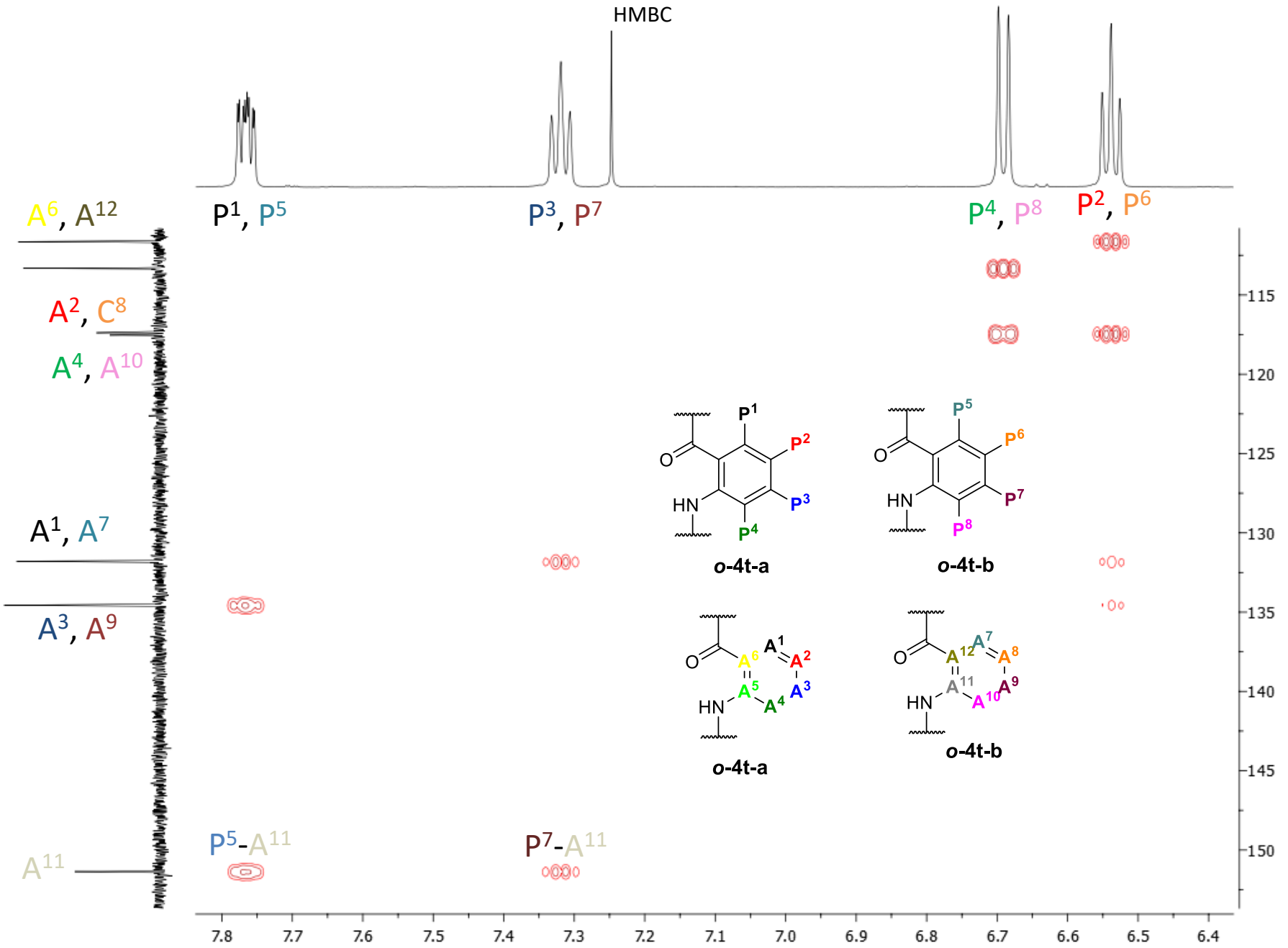
o-4t-b



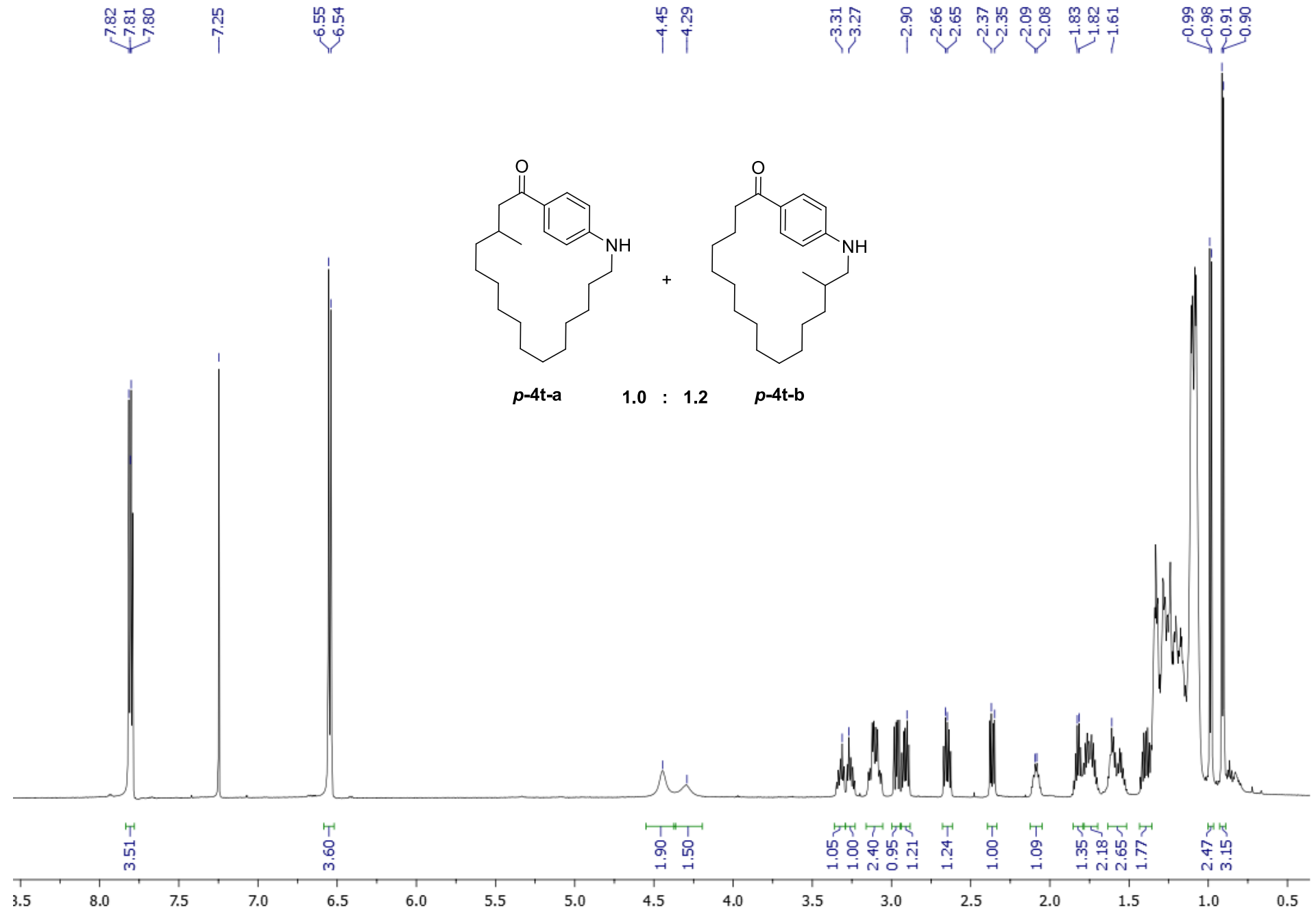
o-4t-a

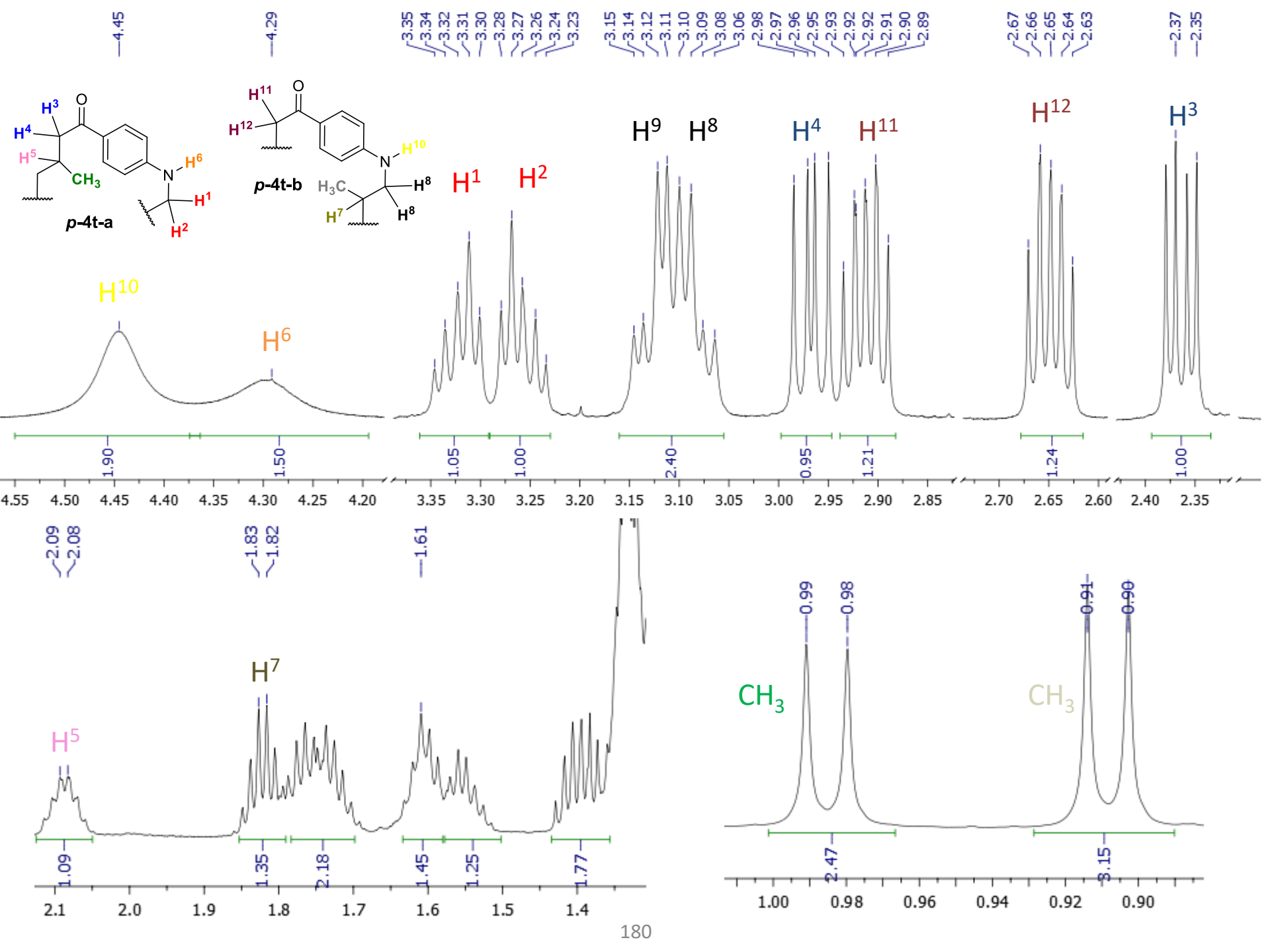


o-4t-b

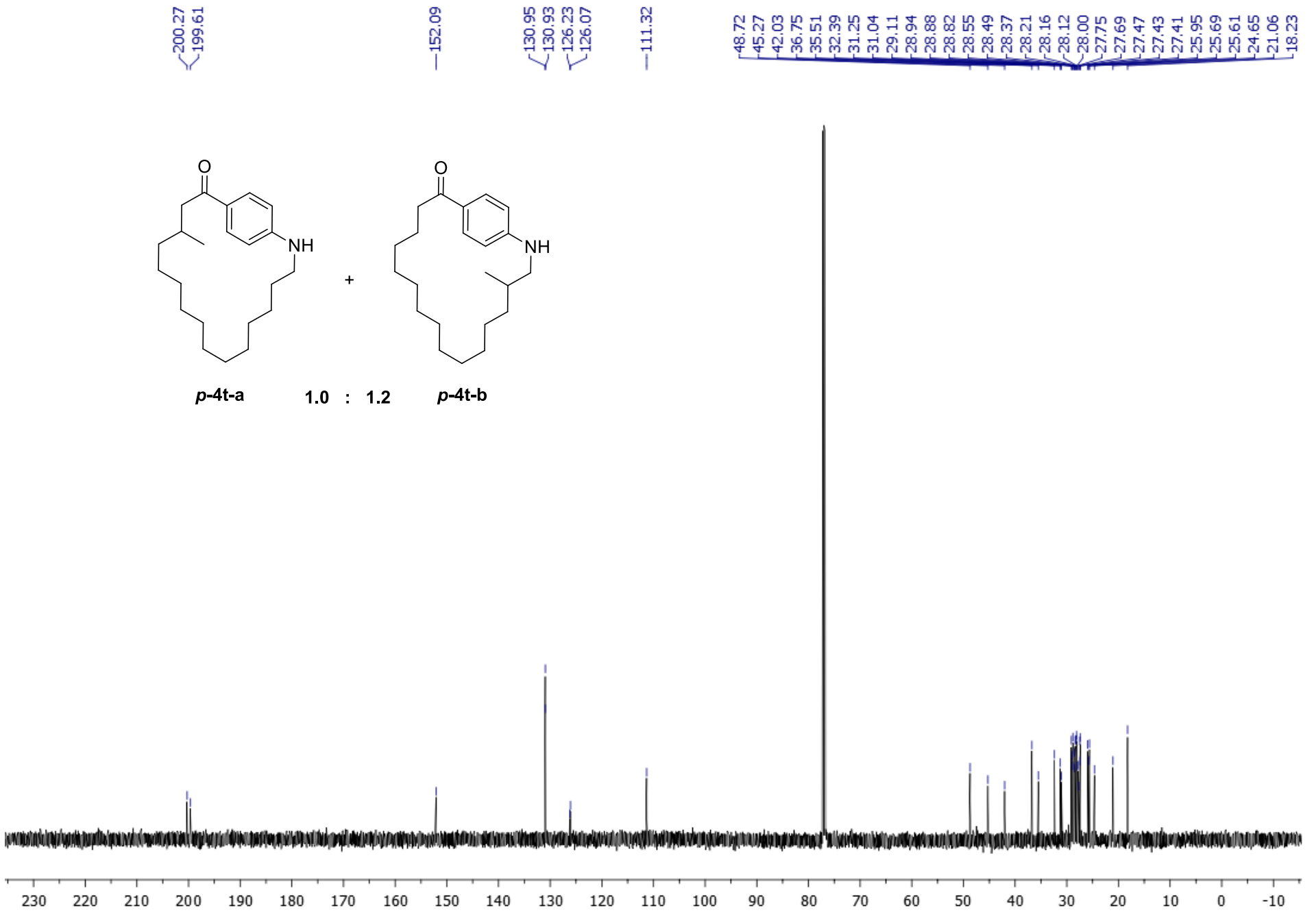

HMBC
A6, A12
P1, P5
P3, P7
P4, P8
P2, P6
A2, C8
A4, A10
A1, A7
A3, A9
A11
P5-A11
P7-A11
o-4t-a
o-4t-b
o-4t-a
o-4t-b
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
6.4
115
120
125
130
135
140
145
150
f1 (ppm)

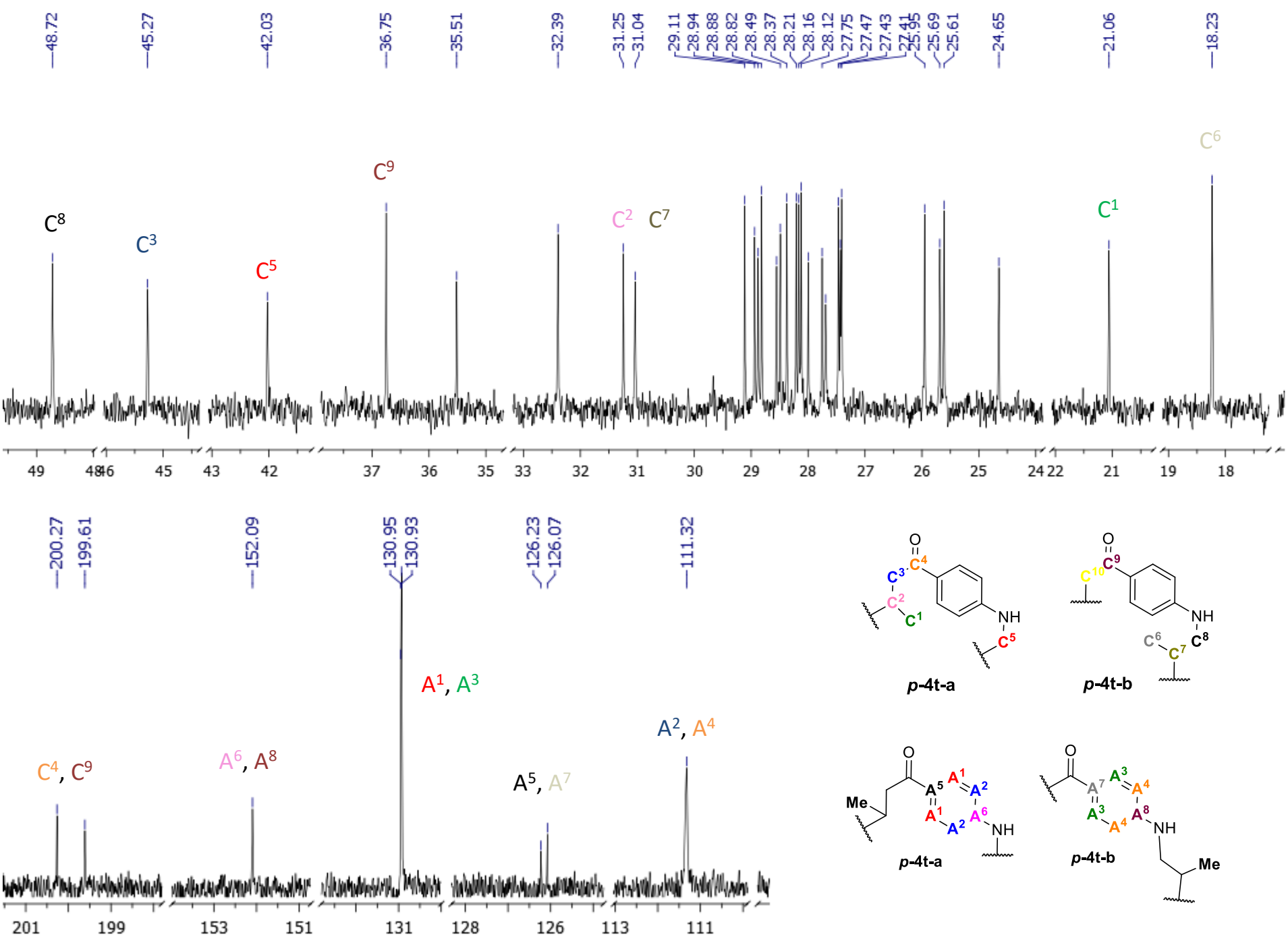
^{1}H NMR (600 MHz, chloroform-*d*)

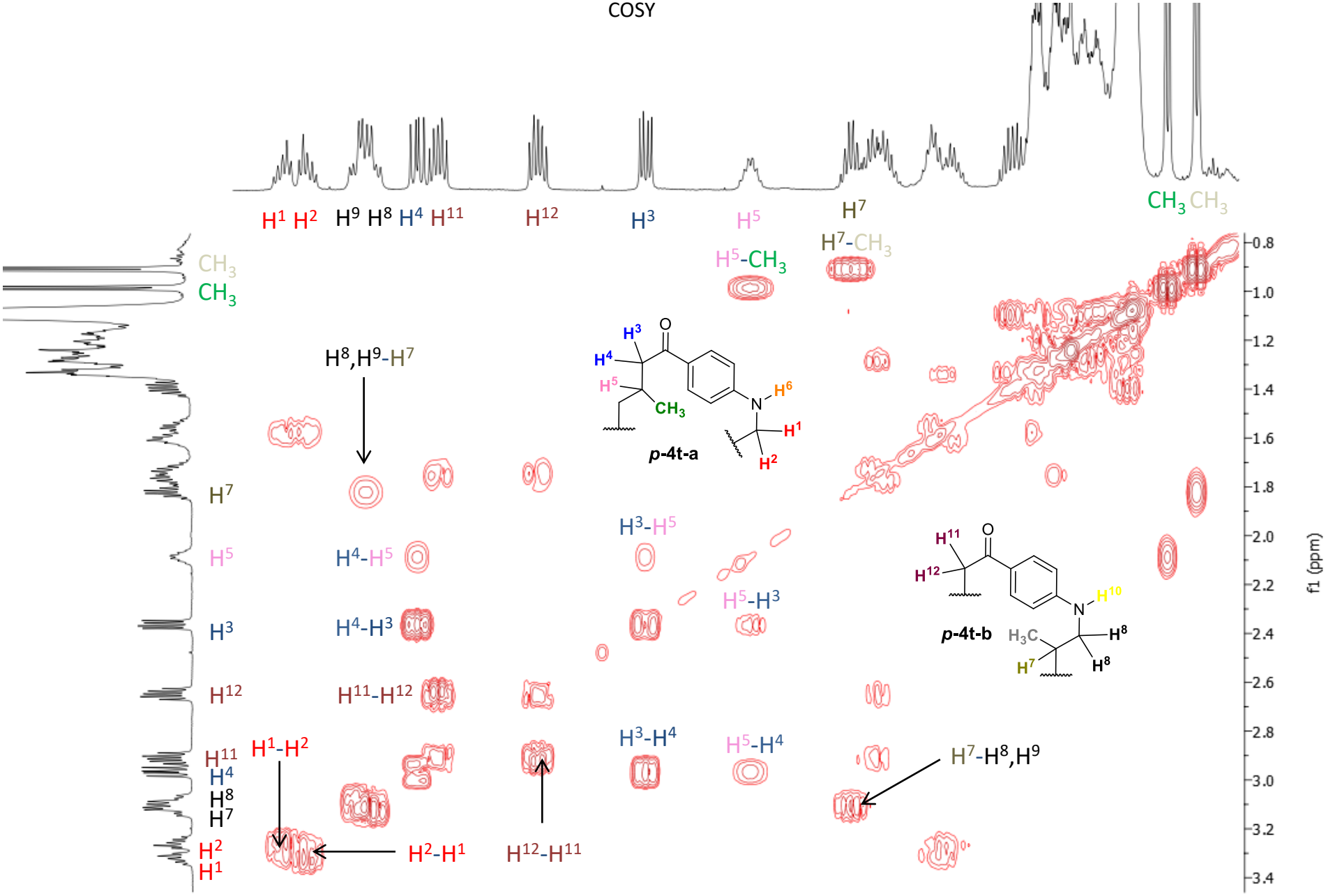



p-4t-a
p-4t-b
H1
H2
H3
H4
H5
H6
H7
H8
H9
H10
H11
H12
CH3
CH3

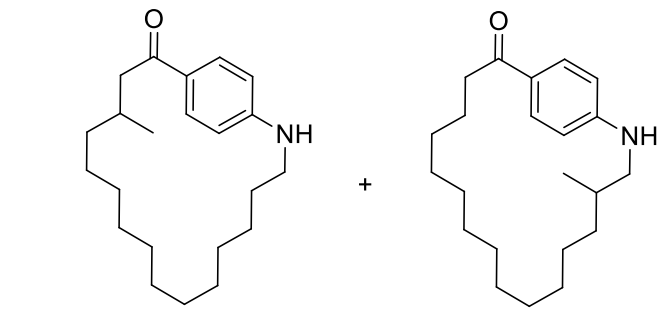
^{13}C NMR (151 MHz, chloroform-*d*)




48.72
45.27
42.03
36.75
35.51
32.39
31.25
31.04
29.11
28.94
28.88
28.82
28.49
28.37
28.21
28.16
28.12
27.75
27.47
27.43
27.41
25.95
25.69
25.61
24.65
21.06
18.23
C8
C3
C5
C9
C2
C7
C1
C6
49
48
46
45
43
42
37
36
35
33
32
31
30
29
28
27
26
25
24
22
21
19
18
200.27
199.61
152.09
130.95
130.93
126.23
126.07
111.32
C4, C9
A6, A8
A1, A3
A5, A7
A2, A4
201
199
153
151
131
128
126
113
111
p-4t-a
p-4t-b
p-4t-a
p-4t-b

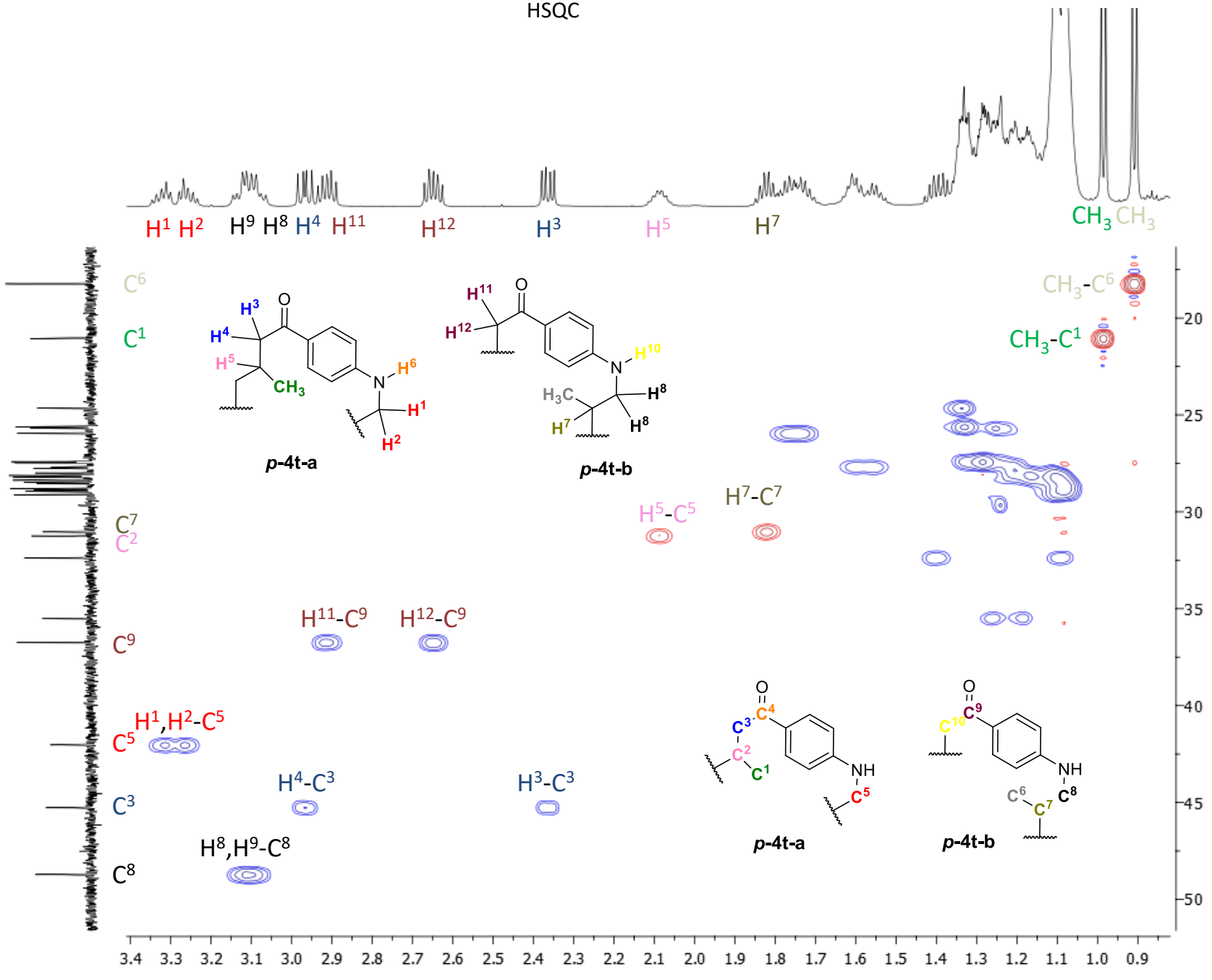

COSY
H1 H2
H9 H8 H4 H11
H12
H3
H5
H7
CH3 CH3
H7-CH3
H5-CH3
H8,H9-H7
H3-H5
H4-H5
H5-H3
H4-H3
H11-H12
H3-H4
H5-H4
H7-H8,H9
H1-H2
H2-H1
H12-H11
p-4t-a
p-4t-b
f1 (ppm)

HSQC

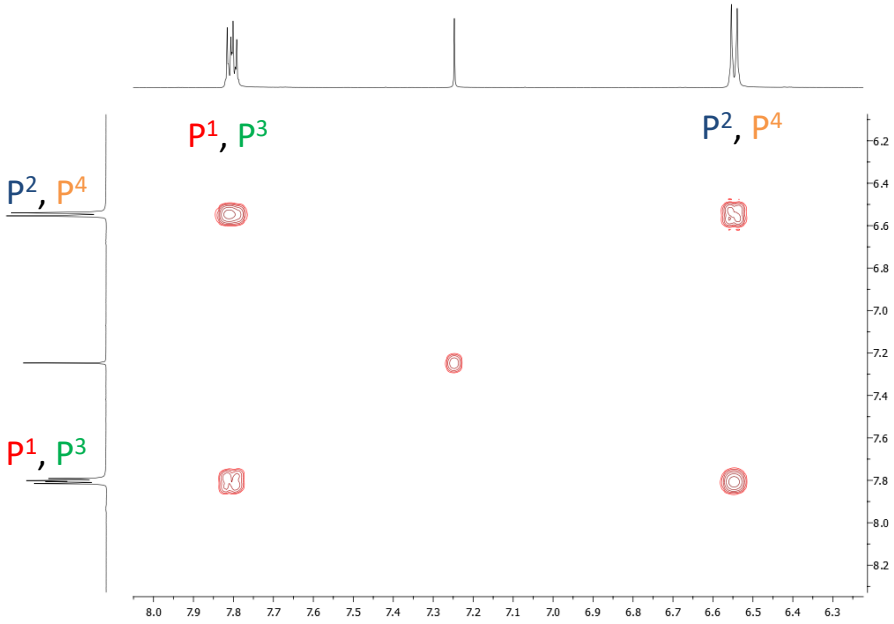


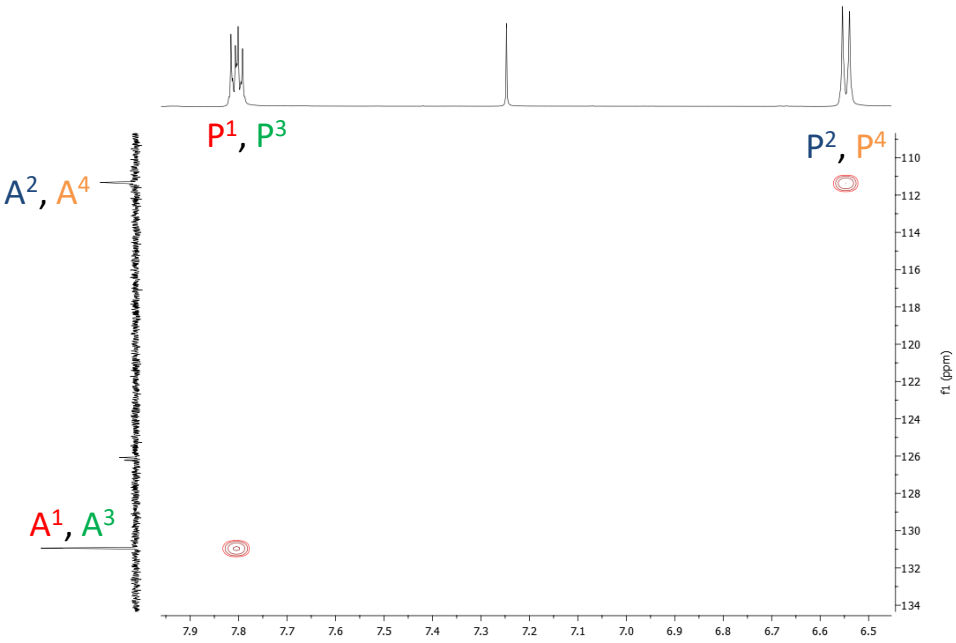
p-4t-a 1.0 : 1.2 *p*-4t-b

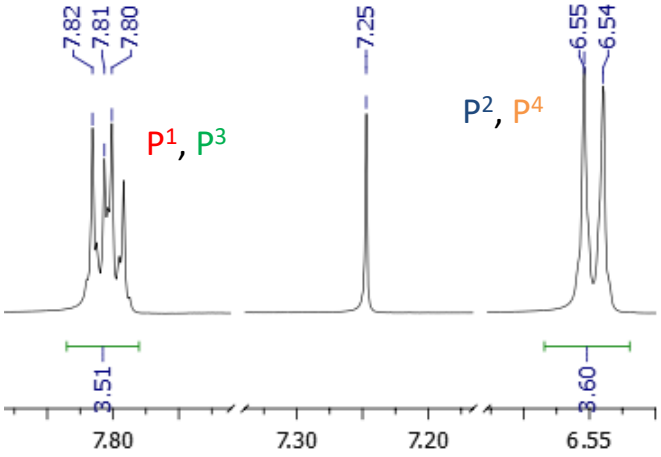
f1 (ppm)

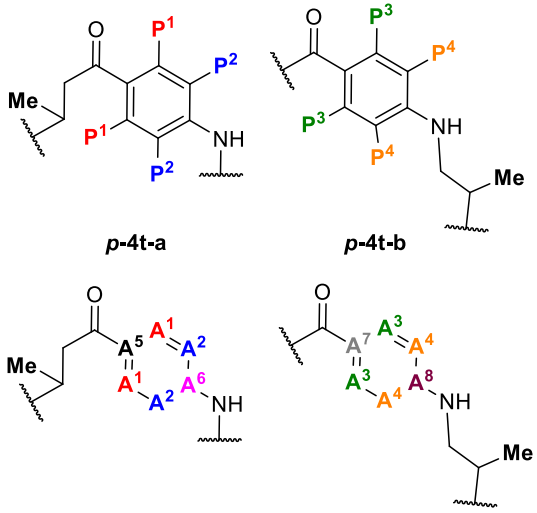

HSQC
H1 H2
H9 H8 H4 H11
H12
H3
H5
H7
CH3 CH3
C6
C1
C7
C2
C9
C5
C3
C8
H1,H2-C5
H4-C3
H8,H9-C8
H11-C9
H12-C9
H3-C3
H5-C5
H7-C7
CH3-C6
CH3-C1
p-4t-a
p-4t-b
p-4t-a
p-4t-b
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9
20 25 30 35 40 45 50
f1 (ppm)

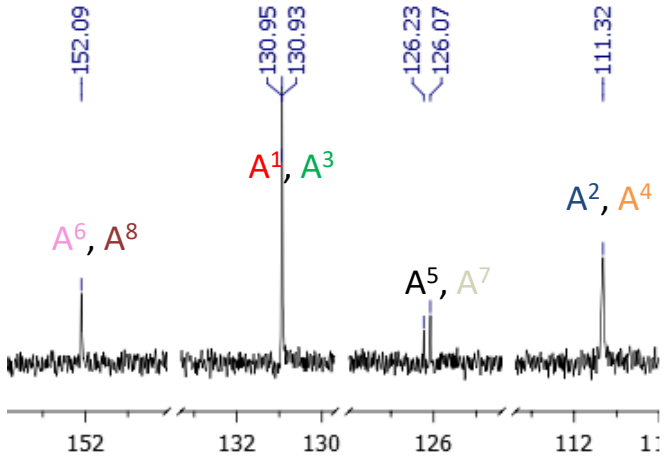
COSY, HSQC


P1, P3
P2, P4
P2, P4
P1, P3


P1, P3
P2, P4
A2, A4
A1, A3
f1 (ppm)


7.82
7.81
7.80
7.25
6.55
6.54
P1, P3
P2, P4
3.51
3.60
7.80
7.30
7.20
6.55


Me
NH
p-4t-a
p-4t-b


152.09
130.95
130.93
126.23
126.07
111.32
A1, A3
A2, A4
A6, A8
A5, A7
152
132
130
126
112