Supporting Information

One-pot Oximation-Beckmann Rearrangement under Mild, Aqueous Micellar Conditions

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1. General Information

1.1. Practical Considerations

Unless otherwise stated, all reactions were performed in oven-dried 5 mL glass V-vials or reaction flask equipped with a PTFE-coated magnetic stir bar. All experiments were monitored by analytical pre-coated silica gel plates thin layer chromatography (TLC). After elution, plate was visualized under UV illumination at 254 nm for UV active materials, followed by staining with alkaline potassium permanganate or using cerium ammonium molybdate solution with subsequent charring on a hot plate for enhanced visualization. Solvents were removed under reduced pressure and gently heated in a water bath at 40 °C. Column chromatography was conducted using 100–200 mesh silica gel, with columns packed as slurry in hexanes and equilibrated with the appropriate solvent mixture before use.

1.2. Materials

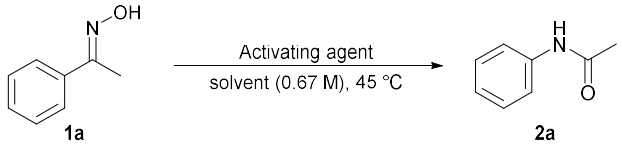
Materials obtained from commercial suppliers were used without further purification. All surfactant solutions were prepared in the Type I water from Milli-Q system (Direct-Q® 3) was used for reactions and extractions while all other solvents for chromatography were of LR grade. Analytical thin-layer chromatography (TLC) was executed on Silica gel 60 F_{254} pre-coated plates. NMR solvents such as chloroform-d ($CDCl_3$), and dimethyl sulfoxide-d_6 (DMSO-d_6) were obtained from Sigma-Aldrich. Acetophenone oxime (**1a**) for initial optimization was prepared according to the literature known procedure.[1]

1.3. Instrumentation

For routine analysis, liquid chromatography-mass spectrometry (LC-MS) was performed using LC-Q-ToF Waters Synapt. High-resolution mass spectrometry (HRMS) was recorded using Agilent UHD 6540 LC-Q-TOF mass spectrometer with electrospray ionization (ESI). Routine NMR spectra (^{1}H NMR, ^{13}C NMR and DEPT) were recorded on Bruker 400 MHz spectrometer. Spectral data include chemical shifts (multiplicity, coupling constants in Hz, integration). Chemical shifts are in ppm (δ), and ^{1}H resonances are referenced to residual solvent peaks for $CDCl_3$ (7.26 ppm) or DMSO-d_6 (2.50 ppm). ^{13}C NMR spectra were recorded with proton decoupling and resonances reported in ppm relative to solvent peaks for $CDCl_3$ (77.06 ppm) or DMSO-d_6 (39.52 ppm). Melting points are uncorrected and recorded using digital melting point apparatus.

2. Optimization Studies

2.1. Optimization for the Beckmann Rearrangement



entry[a]	solvent	activating agent	% yield[b]
1	2 wt % TPGS-750-M	CF_3COOH	trace[c]
2	2 wt % TPGS-750-M	Pivaloyl chloride	trace[c]
3	2 wt % TPGS-750-M	CH_3COOH	0
4	2 wt % TPGS-750-M	PhCOOH	0
5	2 wt % TPGS-750-M	*p*-TsCl	69
6	2 wt % TPGS-750-M	MsCl	47
7	2 wt % TPGS-750-M	PTSA	0
8	2 wt % TPGS-750-M	$ZnCl_2$	trace[c,d]
9	2 wt % TPGS-750-M	$FeCl_3$•$6H_2O$	trace[c,d]
10	2 wt % Tween-20	*p*-TsCl	42
11	2 wt % Saponin	*p*-TsCl	39
12	2 wt % PS-750-M	*p*-TsCl	70
13	2 wt % Brij® 35	*p*-TsCl	83
14	2 wt % SDS	*p*-TsCl	56
15	2 wt % CTAB	*p*-TsCl	68
16	water	*p*-TsCl	34
17	2 wt % Brij® 35	PTSA	0
18	2 wt % Brij® 35	aq. 2M HCl	0
19	**2 wt % Brij® 35**	***p*-TsCl**	**91[e]**
20	2 wt % Brij® 35	2-MCBA	0[d]

[a]Reaction conditions: 2.0 mmol **1a**, 2.0 mmol activating agent, solvent (3 mL), 45 °C, 2 to 5 hours. [b]Isolated yields. [c]Did not observe the significant product formation by TLC hence not isolated. [d]The reaction was performed using 5.0 mol% of activating agent. [e]The phosphate buffer powder (50 mg) was used as an additive. 2-MCBA = 2-methoxycarbonylphenyl boronic acid.

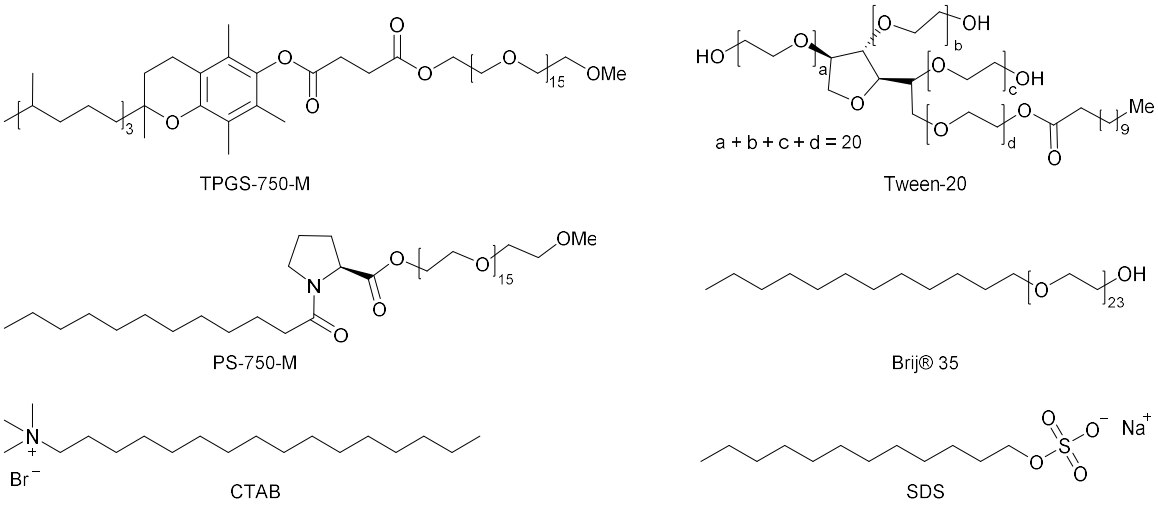
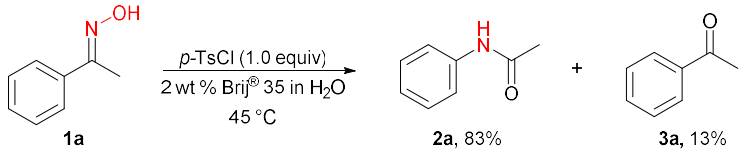


Fig S1: Structures of the surfactants.

2.2. Real-Time pH Monitoring of Reaction



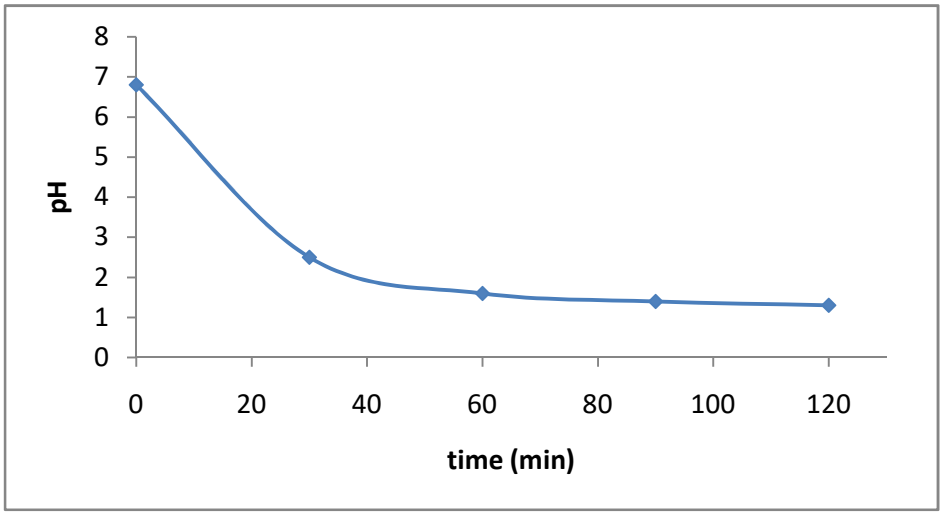
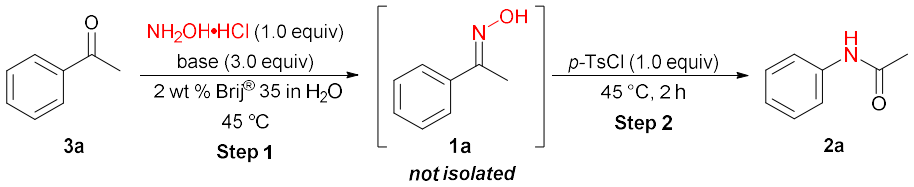


Fig S2: Real-time Monitoring of pH.

2.3. Optimization for One-pot Oximation-Beckmann Rearrangement

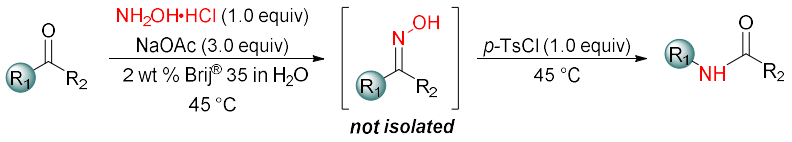


entry[a]	base	% yield[b]
1	NaOAc	89
2	KOAc	83
3	NaOH	36
4	NEt_3	0
5[c]	NaOAc	31
6[d]	NaOAc	65
7[e]	NaOAc	76

[a]Reaction conditions: Step-1: 2.0 mmol acetophenone, 2.0 mmol hydroxylamine hydrochloride, 6.0 mmol base, 2 wt % Brij® 35 (3 mL), 45 °C, 2 to 5 hours. Step-2: 2.0 mmol *p*-TsCl, 45 °C, 2 to 4 hours. [b]Isolated yields. [c]Step-2 was performed using 0.2 equiv. of *p*-TsCl for 4 h. [d]The reaction was performed using 2.0 equiv. of NaOAc. [e]The reactions were performed at 25 °C.

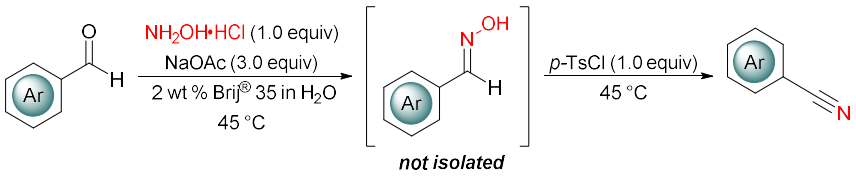
3. General Procedure for One-pot Oximation-Beckmann Rearrangement

3.1. General Procedure for Oximation-Beckmann Rearrangement of Ketones



To a 5 mL screw top V-vial equipped with a PTFE-coated magnetic stir bar, ketone (2.0 mmol), hydroxylamine hydrochloride (2.0 mmol, 1 equiv.), sodium acetate (6.0 mmol, 3 equiv.) and 2 wt % Brij® 35 (3 mL) were added. The reaction vial was fitted with a cap and set to stir for 2-4 h in an aluminum heating block preheated to 45 °C. After complete consumption of the starting material, as monitored by TLC, reaction mixture was cooled to ambient temperature. Subsequently, *p*-TsCl (2.0 mmol, 1 equiv.) was added to the reaction mixture. The vial was capped and set to stir in an aluminum heating block preheated to 45 °C. Upon completion of the reaction (determined by TLC), the mixture was cooled to room temperature, followed by the addition of 2 mL of EtOAc. The mixture was briefly stirred before allowing phase separation. The organic layer was carefully extracted using a pipette, and the extraction was repeated twice for improved recovery. The combined organic layers were dried over anhydrous sodium sulfate, and volatiles were removed under reduced pressure. The resulting crude product was further purified by silica gel column chromatography using EtOAc/hexanes as the eluent.

3.2. General Procedure for Oximation-Beckmann Rearrangement of Aldehydes

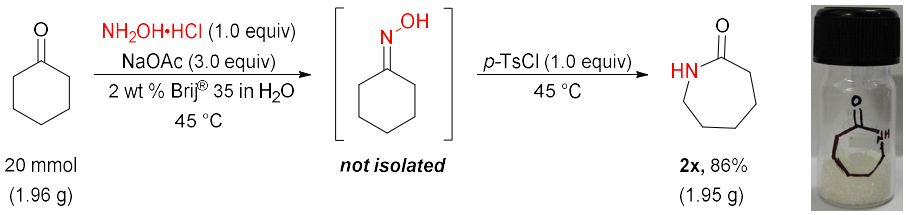


To a 5 mL screw top V-vial equipped with a PTFE-coated magnetic stir bar, aldehyde (2.0 mmol), hydroxylamine hydrochloride (2.0 mmol, 1 equiv.), sodium acetate (6.0 mmol, 3 equiv.) and 2 wt % Brij® 35 (3 mL) were added. The reaction vial was fitted with a cap and set to stir for 2-4 h in an aluminum heating block preheated to 45 °C. After

complete consumption of the starting material, as monitored by TLC, reaction mixture was cooled to ambient temperature. Subsequently, *p*-TsCl (2.0 mmol, 1 equiv.) was added to the reaction mixture. The vial was capped and set to stir in an aluminum heating block preheated to 45 °C. Upon completion of the reaction (determined by TLC), the mixture was cooled to room temperature, followed by the addition of 2 mL of EtOAc. The mixture was briefly stirred before allowing phase separation. The organic layer was carefully extracted using a pipette, and the extraction was repeated twice for improved recovery. The combined organic layers were dried over anhydrous sodium sulfate, and volatiles were removed under reduced pressure. The resulting crude product was further purified by silica gel column chromatography using EtOAc/hexanes as the eluent.

The reaction for isatin was performed using the same procedure as described above.

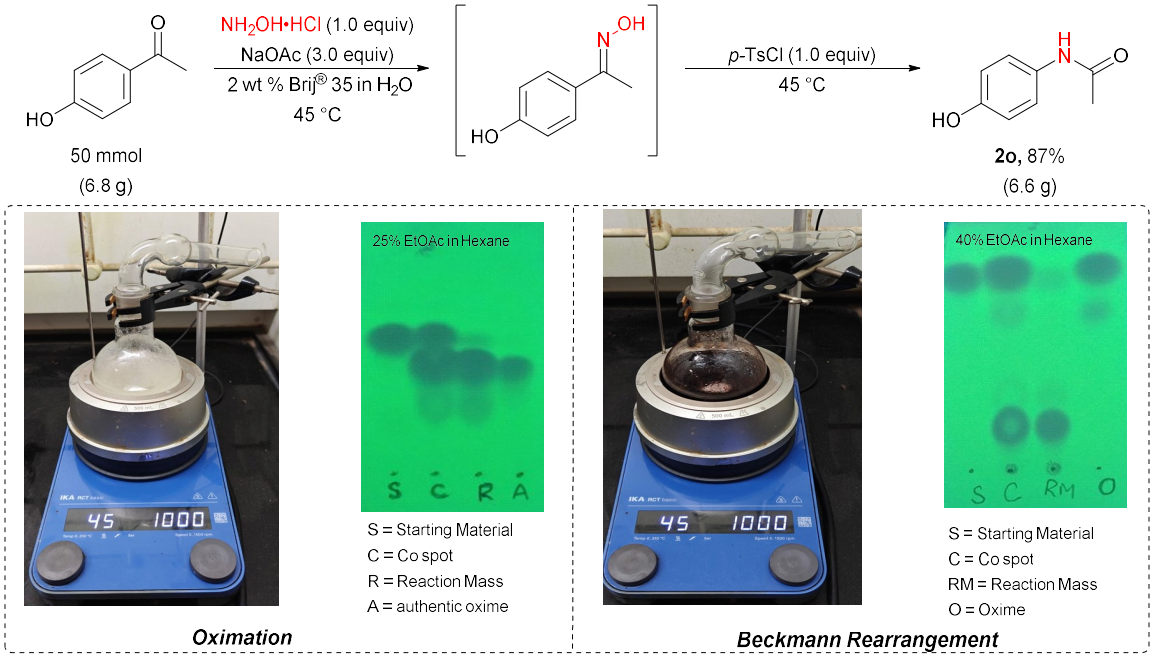
4. Procedure for Gram Scale Synthesis of ε-Caprolactam (2x)



To a 50 mL round-bottom flask equipped with a PTFE-coated magnetic stir bar, cyclohexanone (20.0 mmol, 1.96 g), hydroxylamine hydrochloride (20.0 mmol, 1.39 g), sodium acetate (60.0 mmol, 4.92 g), and 2 wt % Brij® 35 (20 mL) were added. The reaction mass was stirred for 4 hours in an aluminum heating block preheated to 45 °C. After complete consumption of cyclohexanone, as monitored by TLC, the reaction mixture was cooled to ambient temperature. Subsequently, *p*-TsCl (20.0 mmol, 3.80 g) was added to the reaction mixture, and stirring was continued at 45 °C for 2 hours. Upon completion of the reaction (determined by TLC), the mixture was cooled to room temperature, followed by the addition of 20 mL of EtOAc. The mixture was briefly stirred before allowing phase separation. The organic layer was carefully extracted, and the extraction was repeated twice with the same volume of EtOAc. The combined organic layers were dried over anhydrous sodium sulfate, and volatiles were removed under

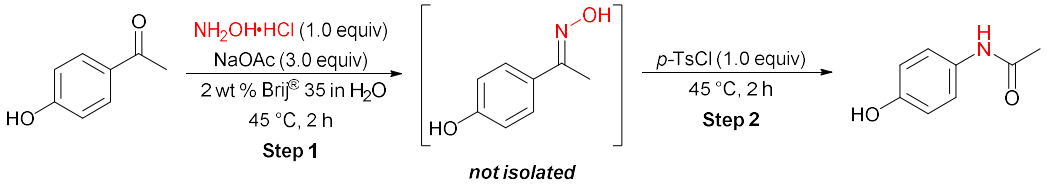
reduced pressure. The resulting crude product was further purified by silica gel column chromatography using EtOAc/hexanes as the eluent, affording ε-caprolactam (1.95 g, 86%) as a white solid.

5. Procedure for Gram Scale Synthesis of Paracetamol (2o)



To a 250 mL round-bottom flask equipped with a PTFE-coated magnetic stir bar, 4-Hydroxyphenylethanone (50.0 mmol, 6.81 g), hydroxylamine hydrochloride (50.0 mmol, 3.47 g), sodium acetate (150.0 mmol, 12.30 g), and 2 wt % Brij® 35 (68 mL) were added. The reaction mass was stirred for 3 hours in an aluminum heating block preheated to 45 °C. After complete consumption of 4-Hydroxyphenylethanone, as monitored by TLC, the reaction mixture was cooled to ambient temperature. Subsequently, *p*-TsCl (50.0 mmol, 9.53 g) was added to the reaction mixture, and stirring was continued at 45 °C for 2 hours. Upon completion of the reaction (determined by TLC), the mixture was cooled to room temperature, followed by the addition of 20 mL of EtOAc. The mixture was briefly stirred before allowing phase separation. The organic layer was carefully extracted, and the extraction was repeated twice with the same volume of EtOAc. The combined organic layers were evaporated under reduced pressure. The resulting crude product was further purified by crystallization in ethanol (6.6 g, 87%) as a white solid.

6. Calculation of the Green Chemistry Metrics for the gram scale synthesis of Paracetamol



Sr. No	Reagents	Mol. Formula	Mol. Wt.	Equiv.	mmol	Quantity in g
1	4'-Hydroxy acetophenone	$C_8H_8O_2$	136.15	1.0	50	6.81
2	Hydroxylamine hydrochloride	$NH_2OH \cdot HCl$	69.49	1.0	50	3.47
3	Sodium acetate	CH_3COONa	82.0343	3.0	150	12.30
4	p-Toluenesulfonyl chloride	$CH_3C_6H_4SO_2Cl$	190.65	1.0	50	9.53
5	Brij® 35	2 wt % in water (68 mL)				1.36
6	Ethyl acetate	Recyclable, hence considering 10% lost as waste				5.41
7	Ethanol	Recyclable, hence considering 10% lost as waste				0.79

Product

Sr. No	Product	Mol. Formula	Mol. Wt.	Quantity in g	% Yield
1	Paracetamol	$C_8H_9NO_2$	151.16	6.60	87.3

- Amount of reagents = (6.81+3.47+12.30+9.53+1.36) g = 33.47 g
- Amount of final product = 6.6 g
- Amount of waste* = (Amount of reagents - Amount of final product) + Solvent loss
  = (33.47 - 6.60) g + 5.41 g + 0.79 g = 33.07 g

$$\text{E-factor} = \frac{\text{Amount of waste}}{\text{Amount of product}} = \frac{33.07\ \text{g}}{6.60\ \text{g}} = 5.0$$

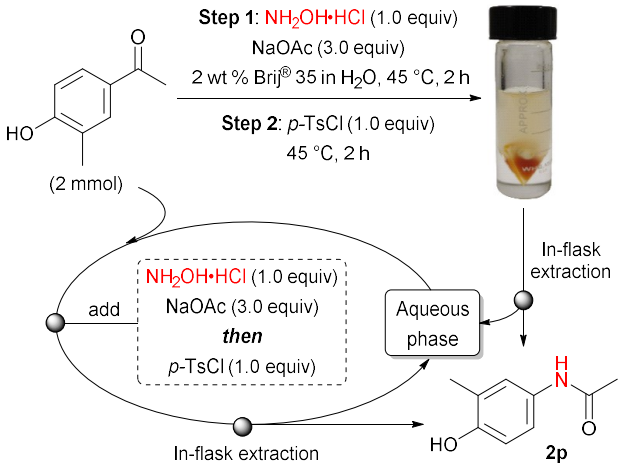
$$\text{PMI} = \frac{\sum \text{Mass (reactants + reagents + surfactant + water + solvents)}}{\text{Mass of Product}}$$

$$= \frac{(6.81 + 3.47 + 12.30 + 9.53 + 68 + 54.12 + 7.9)\ \text{g}}{6.60\ \text{g}} = 24.56$$

$$\text{WWI} = \frac{\sum \text{Mass (process water)}}{\text{Amount of product}} = \frac{66.64\ \text{g}}{6.6\ \text{g}} = 10.1$$

* For E-factor calculation, the loss of recyclable solvents (EtOAc, ethanol) was considered to be 10%.[2]

7. Recycling of the Reaction Medium



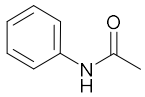
Initial run: To a 5 mL screw top V-vial equipped with a PTFE-coated magnetic stir bar, 4-Hydroxy-3-methylacetophenone (2.0 mmol, 300 mg), hydroxylamine hydrochloride (1 equiv.), sodium acetate (3 equiv.) and 2 wt % Brij® 35 (3 mL) were added. The reaction vial was fitted with a cap and set to stir for 2 h in an aluminum heating block preheated to 45 °C. After complete consumption of the starting material, as monitored by TLC, reaction mixture was cooled to ambient temperature. Subsequently, *p*-TsCl (1 equiv.) was added to the reaction mixture. The vial was capped and set to stir in an aluminum heating block preheated to 45 °C. Upon completion of the reaction (determined by TLC), the mixture was cooled to room temperature, followed by the addition of 2 mL of EtOAc. The mixture was briefly stirred before allowing phase separation. The organic layer was carefully extracted using a pipette, and the extraction was repeated twice for improved recovery. The aqueous solution was retained for recycle. The combined organic layers were dried over anhydrous sodium sulfate, and volatiles were removed under reduced pressure. The resulting crude product was further purified by silica gel column chromatography using EtOAc/hexanes as the eluent, affording **2p** as off white solid; R_f = 0.29 (2:3; EtOAc:Hexanes); yield 91% (300 mg). Solvents used in silica gel chromatography was recovered and reused.

1st recycle: 4-Hydroxy-3-methylacetophenone (2.0 mmol, 300 mg), hydroxylamine hydrochloride (1 equiv.) and sodium acetate (3 equiv.) were added to the recovered aqueous layer. The reaction vial was fitted with a cap and set to stir for 2 h in an aluminum heating block preheated to 45 °C. After complete consumption of the starting material, as monitored by TLC, reaction mixture was cooled to ambient temperature. Subsequently, *p*-TsCl (1 equiv.) was added to the reaction mixture. The vial was capped and set to stir in an aluminum heating block preheated to 45 °C. Upon completion of the reaction (determined by TLC), the mixture was cooled to room temperature, followed by the addition of 2 mL of EtOAc. The mixture was briefly stirred before allowing phase separation. The organic layer was carefully extracted using a pipette, and the extraction was repeated twice for improved recovery. The aqueous solution was retained for further recycle. The combined organic layers were dried over anhydrous sodium sulfate, and volatiles were removed under reduced pressure. The resulting crude product was further purified by silica gel column chromatography using EtOAc/hexanes as the eluent, affording **2p** as off white solid; R_f = 0.25 (2:3; EtOAc:Hexanes); yield 89% (294 mg). Solvents used in silica gel chromatography was recovered and reused.

The remaining recycles were performed by employing a procedure as described above. Yield of **2p** after each recycle are: 2nd recycle 90% (298 mg), 3rd recycle 88% (277 mg), 4th recycle 54% (178 mg).

8. Characterization Data

_N_-phenylacetamide (2a)[3]



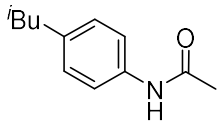
Compound **2a** was synthesized according to the general procedure 3.1 using acetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.43; 30% EtOAc/hexanes); yield: 89%, 241 mg; white solid; m.p. 114-116 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.92 (s, 1H), 7.58 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.37 – 7.23 (m, 2H), 7.06 – 6.99 (m, 1H), 2.04 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.26, 139.34, 128.66, 122.96, 118.96, 24.01.

***N*-(4-Isobutylphenyl)acetamide (2b)**[4]



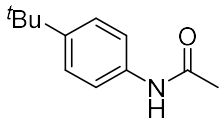
Compound **2b** was synthesized according to the general procedure 3.1 using 4′-isobutylacetophenone, on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.54; 50% EtOAc/hexanes); yield: 88%, 337 mg; light yellow solid; m.p. 125-127 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.84 (s, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 2.36 (d, *J* = 7.2 Hz, 2H), 2.01 (s, 3H), 1.82 – 1.72(m, 1H), 0.83 (d, *J* = 6.4 Hz, 6H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 168.05, 137.10, 135.70, 129.04, 118.89, 44.06, 29.70, 23.95, 22.13.

***N*-(4-tert-Butylphenyl)acetamide (2c)**[5]



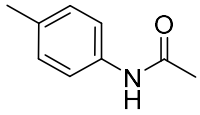
Compound **2c** was synthesized according to the general procedure 3.1 using 4-t-butylacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.37; 50% EtOAc/hexanes); yield: 94%, 360.0 mg; white solid; m.p. 167-169 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.84 (s, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 2.01 (s, 3H), 1.24 (s, 9H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 168.02, 145.23, 136.75, 125.22, 118.79, 33.96, 31.21, 23.90.

***N*-*p*-tolylacetamide (2d)**[5]



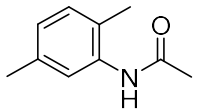
Compound **2d** was synthesized according to the general procedure 3.1 using 4′-methylacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.30; 50% EtOAc/hexanes); yield: 86%, 257 mg; white solid; m.p. 149-151 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.83 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 2.24 (s, 3H), 2.01 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.03, 136.86, 131.82, 129.05, 118.99, 23.96, 20.44.

***N*-(2,5-dimethylphenyl)acetamide (2e)**[6]



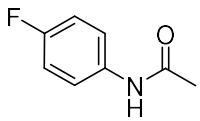
Compound **2e** was synthesized according to the general procedure 3.1 using 2,5-dimethylacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.39; 20% EtOAc/hexanes); yield: 91%, 297 mg; off white solid; m.p. 140-142 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.21 (s, 1H), 7.20 (s, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 1H), 2.23 (s, 3H), 2.13 (s, 3H), 2.03 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.13, 136.31, 134.84, 130.05, 128.39, 125.66, 125.51, 23.30, 20.62, 17.46.

***N*-(4-fluorophenyl)acetamide (2f)**[3]



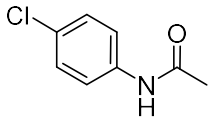
Compound **2f** was synthesized according to the general procedure 3.1 using 4-fluoroacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.26; 50% EtOAc/hexanes); yield: 81%, 248.0 mg; off white solid; m.p. 152-154 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.98 (s, 1H), 7.60 – 7.56 (m, 2H), 7.14 – 7.10 (m, 2H), 2.02 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.14, 159.01, 156.60, 135.75, 135.73, 120.71, 120.64, 115.31, 115.09, 23.87.

N-(4-chlorophenyl)acetamide (2g)[5]



Compound **2g** was synthesized according to the general procedure 3.1 using 4-chloro acetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

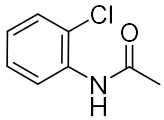
(R_f = 0.32; 50% EtOAc/hexanes); yield: 83%, 282 mg; white solid; m.p. 178-180 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.07 (s, 1H), 7.60 (d, *J* = 9.2 Hz, 2H), 7.34 (d, J = 9.2 Hz, 2H), 2.04 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.44, 138.26, 128.56, 126.48, 120.47, 23.97.

HRMS (**ESI**) m/z: calcd for C_8H_7ONCl $[M+H]^+$ 168.0216, found 168.0214.

N-(2-chlorophenyl)acetamide (2h)[7]



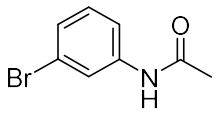
Compound **2h** was synthesized according to the general procedure 3.1 using 2-chloro acetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.4; 50% EtOAc/hexanes); yield: 79%, 268 mg; white solid; m.p. 87-89 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.53 (s, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.47 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.31 (td, *J* = 8.0, 1.6 Hz, 1H), 7.17 (td, *J* = 7.6, 1.6 Hz, 1H), 2.09 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 169.69, 135.10, 129.47, 127.38, 126.49, 126.36, 126.22, 23.37.

N-(3-bromophenyl)acetamide (2i)[8]



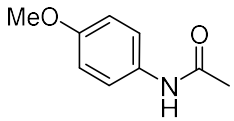
Compound **2i** was synthesized according to the general procedure 3.1 using 3-bromoacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.57; 50% EtOAc/hexanes); yield: 85%, 364 mg; light yellow solid; m.p. 85-87 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.10 (s, 1H), 7.94 (t, *J* = 1.8 Hz, 1H), 7.46 – 7.44 (m, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.21 – 7.19 (m, 1H), 2.04 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.69, 140.19, 130.71, 125.59, 121.53, 121.24, 117.67, 24.05.

N-(4-methoxyphenyl)acetamide (2j)[3]



Compound **2j** was synthesized according to the general procedure 3.1 using 4-methoxyacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

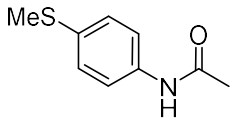
(R_f = 0.49; 70% EtOAc/hexanes); yield: 95%, 314.0 mg; off white solid; m.p. 130-132 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.77 (s, 1H), 7.48 (d, *J* = 9.1 Hz, 2H), 6.85 (d, *J* = 9.1 Hz, 2H), 3.70 (s, 3H), 1.99 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 167.71, 155.01, 132.53, 120.53, 113.77, 55.12, 23.78.

HRMS (**ESI**) m/z: calcd for $C_9H_{12}O_2N$ $[M+H]^+$ 166.0868, found 166.0863.

***N*-(4-(methylthio)phenyl)acetamide (2k)**



Compound **2k** was synthesized according to the general procedure 3.1 using 4-(methylthio)acetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

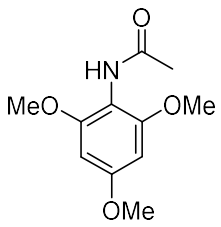
(R_f = 0.37; 50% EtOAc/hexanes); yield: 93%, 338 mg; off white solid; m.p. 127-129 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.94 (s, 1H), 7.53 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 2.43 (s, 3H), 2.02 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 168.22, 136.91, 131.41, 127.18, 119.68, 23.99 15.61.

HRMS (**ESI**) m/z: calcd for $C_9H_{10}ONS$ $[M-H]^-$ 180.0483, found 180.0486.

***N*-(2,4,6-trimethoxyphenyl)acetamide (2l)**



Compound **2l** was synthesized according to the general procedure 3.1 using 2-4-6-trimethoxyacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

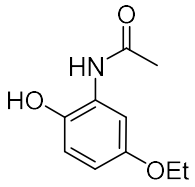
(R_f = 0.28; 80% EtOAc/hexanes); yield: 82%, 369 mg; off white solid; m.p. 138-140 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 8.62 (s, 1H), 6.23 (s, 2H), 3.77(s, 3H), 3.70 (s, 6H), 1.91 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 168.25, 159.19, 156.60, 107.94, 90.93, 55.64, 55.36, 22.68.

HRMS (**ESI**) m/z: calcd for $C_{11}H_{15}O_4NNa$ $[M+Na]^+$ 248.0899, found 248.0890.

***N*-(5-ethoxy-2-hydroxyphenyl)acetamide (2m)**



Compound **2m** was synthesized according to the general procedure 3.1 using 5-ethoxy-2-hydroxyacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

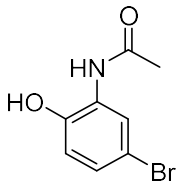
(R_f = 0.40; 50% EtOAc/hexanes); yield: 84%, 328 mg; brown solid; m.p. 154-156 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.25 (d, *J* = 4.4 Hz, 2H), 7.40 (d, *J* = 2.8 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.50 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.88 (q, *J* = 6.8 Hz, 2H), 2.08 (s, 3H), 1.27 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 169.02, 151.15, 141.26, 127.01, 115.94, 109.88, 108.54, 63.29, 23.78, 14.82.

HRMS (**ESI**) m/z: calcd for $C_{10}H_{12}O_3N$ $[M-H]^-$ 194.0817, found 194.0818.

***N*-(5-bromo-2-hydroxyphenyl)acetamide (2n)**[9]



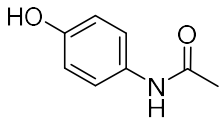
Compound **2n** was synthesized according to the general procedure 3.1 using 5-bromo-2-hydroxyacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.43; 50% EtOAc/hexanes); yield: 83%, 382 mg; light yellow solid; m.p. 175-177 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 10.15 (s, 1H), 9.26 (s, 1H), 8.06 (d, *J* = 2.4 Hz, 1H), 7.06 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.80 (d, *J* = 8.6 Hz, 1H), 2.09 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 169.07, 146.73, 128.20, 126.40, 123.83, 116.93, 109.64, 23.78.

Paracetamol (2o)[3]



Compound **2o** was synthesized according to the general procedure 3.1 using 4-hydroxyacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

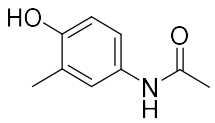
(R_f = 0.17; 40% EtOAc/hexanes); yield: 86%, 260 mg; off white solid; m.p. 168-170 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.64 (s, 1H), 9.13 (s, 1H), 7.33 (d, *J* = 8.8 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 1.97 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 167.57, 153.14, 131.06, 120.84, 115.02, 23.77.

HRMS (**ESI**) m/z: calcd for $C_8H_{10}O_2N$ $[M+H]^+$ 152.0712, found 152.0716.

***N*-(4-hydroxy-3-methylphenyl)acetamide (2p)**



Compound **2p** was synthesized according to the general procedure 3.1 using 4-hydroxy-3-methyl acetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

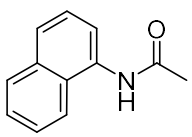
(R_f = 0.29; 40% EtOAc/hexanes); yield: 91%, 301 mg; light brown solid; m.p. 179-181 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.57 (s, 1H), 9.02 (s, 1H), 7.23 (d, *J* = 2.3 Hz, 1H), 7.15 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.66 (d, *J* = 8.2 Hz, 1H), 2.07 (s, 3H), 1.96 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 167.50, 151.23, 130.88, 123.63, 122.14, 118.08, 114.35, 23.78, 16.20.

HRMS (**ESI**) m/z: calcd for $C_9H_{12}O_2N$ $[M+H]^+$ 166.0868, found 166.0866.

***N*-(naphthalen-1-yl)acetamide (2q)**[10]



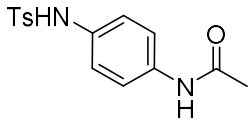
Compound **2q** was synthesized according to the general procedure 3.1 using 1-acetylnaphthalene on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.27; 50% EtOAc/hexanes); yield: 89%, 330 mg; off white solid; m.p. 160-162 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.91 (s, 1H), 8.09 – 8.07 (m, 1H), 7.93 (dd, *J* = 6.8, 4.0 Hz, 1H), 7.72 (dd, *J* = 22.8, 8.4 Hz, 3H), 7.55- 7.46 (m, 4H), 2.19 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.91, 133.69, 128.09, 127.65, 125.95, 125.72, 125.54, 125.02, 122.72, 121.50, 23.47.

N-(4-((4-methylphenyl)sulfonamido)phenyl)acetamide (2r)



Compound **2r** was synthesized according to the general procedure 3.1 using N-(4-acetylphenyl)-p-toluenesulfonamide on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

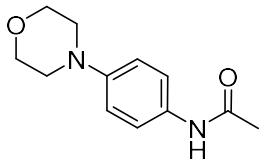
(R_f = 0.25; 60% EtOAc/hexanes); yield: 92%, 560 mg; white solid; m.p. 183-185 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.99 (s, 1H), 9.85 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 9.2 Hz, 2H), 2.32 (s, 3H), 1.98 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.06, 143.10, 136.60, 135.96, 132.55, 129.61, 126.73, 121.42, 119.69, 23.86, 20.96.

HRMS (**ESI**) m/z: calcd for $C_{15}H_{16}O_3N_2SNa$ $[M+Na]^+$ 327.0779, found 327.0769.

N-(4-morpholinophenyl)acetamide (2s)[11]



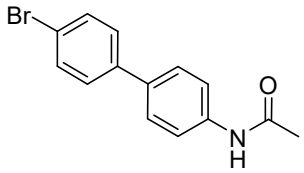
Compound **2s** was synthesized according to the general procedure 3.1 using 4-marpholinoacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.38; 50% EtOAc/hexanes); yield: 93%, 409 mg; light yellow solid; m.p. 209-211 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.71 (s, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 3.71(t, *J* = 6.0 Hz, 4H), 3.01 (t, *J* = 6.0 Hz, 4H), 1.99 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 167.67, 147.05, 131.77, 120.14, 115.49, 66.16, 49.03, 23.84.

N-(4'-bromo-[1,1'-biphenyl]-4-yl)acetamide (2t)



Compound **2t** was synthesized according to the general procedure 3.1 using 4-(bromophenyl)acetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

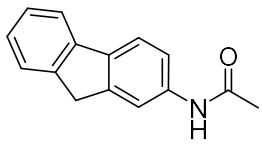
(R_f = 0.25; 50% EtOAc/hexanes); yield: 78%, 453 mg; off white solid; m.p. 238-240 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.06 (s, 1H), 7.68 – 7.65 (m, 2H), 7.62 – 7.60 (m, 2H), 2.06 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.45, 139.20, 138.94, 133.27, 131.77, 128.31, 126.88, 120.34, 119.35, 24.09.

HRMS (**ESI**) m/z: calcd for $C_{14}H_{11}ONBr$ $[M-H]^-$ 288.0024, found 288.0023.

N-(9H-fluoren-2-yl)acetamide (2u)[12]



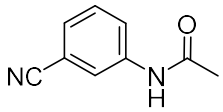
Compound **2u** was synthesized according to the general procedure 3.1 using 2-acetylfluorene on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.57; 50% EtOAc/hexanes); yield: 75%, 335 mg; off white solid; m.p. 192-193 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.02 (s, 1H), 7.92 (d, *J* = 1.0 Hz, 1H), 7.82 – 7.77 (m, 2H), 7.52 (dd, *J* = 13.4, 5.0 Hz, 2H), 7.34 (t, *J* = 7.0 Hz, 1H), 7.25 (td, J = 7.4, 1.1 Hz, 1H), 3.89 (s, 2H), 2.07 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 168.22, 143.72, 142.76, 141.05, 138.45, 136.11, 126.72, 126.03, 125.01, 120.09, 119.39, 117.75, 115.78, 36.51, 24.10.

***N*-(3-cyanophenyl)acetamide (2v)**[13]



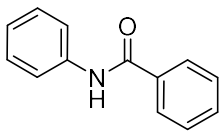
Compound **2v** was synthesized according to the general procedure 3.1 using 3-cyanoacetophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.29; 50% EtOAc/hexanes); yield: 62%, 199 mg; white solid; m.p. 129-131 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 10.28 (s, 1H), 8.07 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.53 – 7.47 (m, 2H), 2.07 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 168.97, 140.06, 130.21, 126.54, 123.47, 121.54, 118.76, 111.51, 24.01.

***N*-phenylbenzamide (2w)**[3]



Compound **2w** was synthesized according to the general procedure 3.1 using benzophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

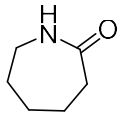
(R_f = 0.40; 20% EtOAc/hexanes); yield: 96%, 379 mg; off white solid; m.p. 162-164 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 10.25 (s, 1H),7.97– 7.95 (m, 2H), 7.80 – 7.79 (m, 2H), 7.60 – 7.52 (m, 3H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.11 (t, *J* = 7.6 Hz, 1H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 165.60, 139.21, 135.00, 131.59, 128.64, 128.42, 127.69, 123.69, 120.40.

HRMS (**ESI**) m/z: calcd for $C_{13}H_{12}ON$ $[M+H]^+$ 198.0919, found 198.0922.

ε-Caprolactam (2x)[3]



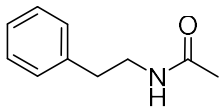
Compound **2x** was synthesized according to the general procedure 3.1 using cyclohexanone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.46; 30% EtOAc/hexanes); yield: 84%, 190 mg; white solid; m.p. 68-70 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.39 (s, 1H), 3.04 (dd, *J* = 10.0, 5.9 Hz, 2H), 2.07 (t, *J* = 4.0 Hz, 2H), 1.68 – 1.62 (m, 2H), 1.57 – 1.41 (m, 4H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 176.93, 41.43, 38.89, 36.41, 29.99, 29.81, 22.97.

***N*-phenethylacetamide (2y)**[14]



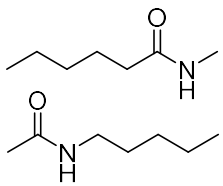
Compound **2y** was synthesized according to the general procedure 3.1 using 4-phenyl-2-butanone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.57; 80% EtOAc/hexanes); yield: 79%, 258 mg; white solid; m.p. 50-51 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.94 (s, 1H), 7.30 – 7.27 (m, 2H), 7.21 – 7.17 (m, 3H), 3.24 (q, *J* = 8 Hz, 2H), 2.69 (t, *J* = 8 Hz, 2H), 1.78 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 169.14, 139.56, 128.64, 128.35, 126.10, 40.25, 35.24, 22.64.

***N*-methylhexanamide ($2z_1$) and N-pentylacetamide ($2z_2$)**[15,16]



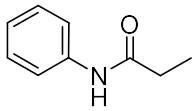
Compound $\mathbf{2z_1}$ and $\mathbf{2z_2}$ was obtained as a mixture (1:1). Synthesis was achieved according to the general procedure 3.1 using 2-heptanone on a 2.0 mmol scale.

(R_f = 0.27; 50% EtOAc/hexanes); yield: 68% (for mixture), 176 mg; light yellow liquid.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 7.78 (s, 1H), δ 7.68 (s, 1H), 2.99 (q, *J* = 7.6 Hz,2H), 2.54 (d, *J* = 4.8 Hz, 3H), 2.02 (t, *J* = 7.6 Hz, 2H), 1.77 (s, 3H), 1.51 – 1.43 (m, 2H), 1.40 – 1.33 (m, 2H), 1.29 – 1.19 (m, 8H), 0.87 – 0.82 (m, 6H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 172.53, 168.91, 38.48, 35.33, 30.98, 28.86, 28.68, 25.41, 24.99, 22.63, 21.92, 21.89, 13.94, 13.89.

N-phenylpropionamide (2aa)[7]



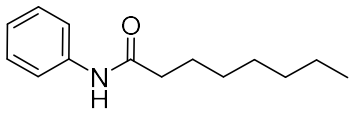
Compound **2aa** was synthesized according to the general procedure 3.1 using propiophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.55; 50% EtOAc/hexanes); yield: 87%, 261 mg; white solid; m.p. 104-106 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.84 (s, 1H), 7.58 (dd, *J* = 8.4, 0.8 Hz, 2H), 7.29 – 7.25 (m, 2H), 7.02 – 6.98 (m, 1H), 2.30 (q, *J* = 7.6 Hz, 2H), 1.08 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 171.96, 139.39, 128.63, 122.87, 118.99, 29.51, 9.67.

N-phenyloctanamide(2ab)



Compound **2ab** was synthesized according to the general procedure 3.1 using octanophenone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

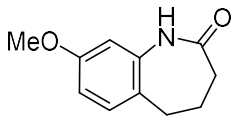
(R_f = 0.50; 50% EtOAc/hexanes); yield: 89%, 390 mg; off white solid; m.p. 82-84 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.84 (s, 1H), 7.59 – 7.56 (m, 2H), 7.29 – 7.25 (m, 2H), 7.02 – 6.98 (m, 1H), 2.28 (t, *J* = 7.2 Hz, 2H), 1.59 – 1.55 (m, 2H), 1.27 – 1.23 (m, 9H), 0.85 (t, *J* = 6.4 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 171.26, 139.38, 128.63, 122.89, 119.00, 36.43, 31.20, 28.66, 28.50, 25.15, 22.09, 13.95.

HRMS (**ESI**) m/z: calcd for $C_{14}H_{20}ON$ $[M-H]^-$ 218.1545, found 218.1549.

8-methoxy-1,3,4,5-tetrahydro-2H-benzo[b]azepin-2-one (ac)[17]



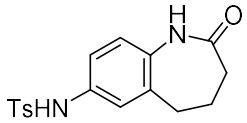
Compound **2ac** was synthesized according to the general procedure 3.1 using 7-methoxy-1-tetralone on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.47; 40% EtOAc/hexanes); yield: 67%, 256 mg; white solid; m.p. 132-134 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.45 (s, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.67 – 6.52 (m, 2H), 3.71 (s, 3H), 2.60 (t, *J* = 7.2 Hz, 2H), 2.15 – 2.02 (m, 4H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 173.43, 158.36, 139.78, 130.33, 125.62, 109.84, 107.42, 55.14, 33.00, 29.05, 28.13.

4-methyl-*N*-(2-oxo-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl)benzenesulfonamide (2ad)



Compound **2ad** was synthesized according to the general procedure 3.1 using 4-methyl-*N*-(5,6,7,8-tetrahydro-5-oxo-2-naphthalenyl)benzenesulfonamide on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

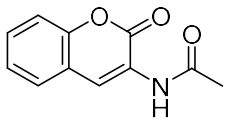
(R_f = 0.40; 50% EtOAc/hexanes); yield: 77%, 509 mg; light brown solid; m.p. 265-267 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 10.07 (s, 1H), 9.34 (s, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.90 – 6.87 (m, 2H), 6.76 (d, *J* = 8.0 Hz, 1H), 2.51 – 2.46 (m, 2H), 2.28 (s, 3H), 2.01 - 1.96 (m, 4H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 173.04, 143.21, 136.64, 135.20, 134.54, 134.22, 129.65, 126.75, 122.32, 121.68, 119.11, 32.68, 29.95, 27.70, 20.97.

HRMS (**ESI**) m/z: calcd for $C_{19}H_{19}O_3N_2S$ $[M+H]^+$ 331.1116, found 331.1106.

***N*-(2-oxo-2H-chromen-3-yl)acetamide (2ae)**



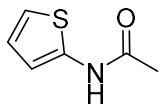
Compound **2ae** was synthesized according to the general procedure 3.1 using 3-acetylcoumarin on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography. (R_f = 0.48; 50% EtOAc/hexanes); yield: 72%, 293 mg; off white solid; m.p. 200-202 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.76 (s, 1H), 8.60 (s, 1H), 7.69 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.51-7.49 (m, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.39-7.30 (m, 1H), 2.17 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 170.26, 157.50, 149.63, 129.54, 127.84, 124.95, 124.59, 123.50, 119.60, 115.81, 23.96.

HRMS (**ESI**) m/z: calcd for $C_{11}H_8O_3N$ $[M-H]^-$ 202.0504, found 202.0502.

***N*-(thiophen-2-yl)acetamide (2af)**[3]



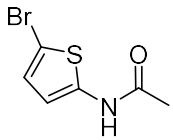
Compound **2af** was synthesized according to the general procedure 3.1 using 2-acetylthiophene on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography. (R_f = 0.54; 50% EtOAc/hexanes); yield: 88%, 249.0 mg; brown solid; m.p. 159-161 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.11 (s, 1H), 6.90 – 6.89 (m, 1H), 6.82 (dd, *J* = 5.6, 3.6 Hz, 1H), 6.61 (dd, *J* = 4.0, 1.6 Hz, 1H), 2.05 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 166.21, 139.91, 123.87, 116.59, 110.24, 22.53.

HRMS (**ESI**) m/z: calcd for C_6H_6ONS $[M-H]^-$ 140.0170, found 140.0166.

***N*-(5-bromothiophen-2-yl)acetamide (2ag)**[18]



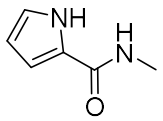
Compound **2ag** was synthesized according to the general procedure 3.1 using 2-acetyl 5-bromo thiophene on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.30; 50% EtOAc/hexanes); yield: 89%, 392 mg; off brown solid; m.p. 135-137 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 11.39 (s, 1H), 6.94 (d, *J* = 4.0 Hz, 1H), 6.41 (d, *J* = 4.0 Hz, 1H), 2.05 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 166.66, 140.36, 126.63, 109.79, 102.40, 22.16.

N-(1H-pyrrol-2-yl)acetamide (2ah)[19]



Compound **2ah** was synthesized according to the general procedure 3.1 using 2-acetylpyrrole on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

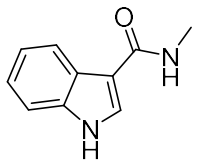
(R_f = 0.40; 50% EtOAc/hexanes); yield: 91%, 226 mg; brown solid; m.p. 156-158 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 11.40 (s, 1H), 7.92 (d, *J* = 4.0 Hz, 1H), 6.82 – 6.80 (m, 1H), 6.70 – 6.69 (m, 1H), 6.06 – 6.04 (m, 1H), 2.72 (d, *J* = 4.4 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 161.20, 126.42, 121.02, 109.44, 108.47, 25.48.

HRMS (**ESI**) m/z: calcd for $C_6H_7ON_2$ $[M-H]^-$ 123.0558, found 123.0562.

N-methyl-1H-indole-3-carboxamide (2ai)



Compound **2ai** was synthesized according to the general procedure 3.1 using 3-acetylindole on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

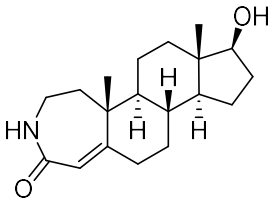
(R_f = 0.32; 25% EtOAc/hexanes); yield: 74%, 256 mg; off white solid; m.p. 195-197 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 11.50 (s, 1H), 8.13 (d, *J* = 7.6 Hz, 1H), 7.94 (d, *J* = 2.2 Hz, 1H), 7.83 (d, *J* = 4.4 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.14 – 7.06 (m, 2H), 2.76 (d, *J* = 4.4 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 165.13, 136.09, 127.41, 121.79, 120.97, 120.25, 111.77, 110.80, 25.56.

HRMS (**ESI**) m/z: calcd for $C_{10}H_{11}ON_2$ $[M+H]^+$ 175.0871, found 175.0865.

17β-Hydroxy-3-aza-A-homoandrost-4α-en-4-one (2aj)[20]



Compound **2aj** was synthesized according to the general procedure 3.1 using testosterone on a 1.0 mmol scale. The crude product was purified by silica gel column chromatography.

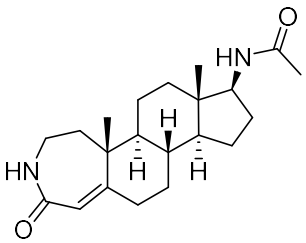
(R_f = 0.17; 10% methanol/DCM); yield: 77%, 234 mg; white solid; m.p. 289-291 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 7.71 (s, 1H), 5.48 (s, 1H), 4.46 (d, *J* = 4.7 Hz, 1H), 3.45 – 3.39 (m, 1H), 3.06 – 2.93 (m, 2H), 2.48 – 2.35 (m, 1H), 2.03 (d, *J* = 12.4 Hz 1H), 1.89 – 1.76 (m, 3H), 1.71 (d, *J* = 12.4 Hz 1H), 1.64 – 1.57 (m, 1H), 1.54 – 1.42 (m, 3H), 1.34 – 1.29 (m, 2H), 1.23 – 1.16 (m, 1H), 1.07 (s, 3H), 0.99 – 0.84 (m, 4H), 0.65 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 168.14, 159.03, 119.56, 79.85, 69.80, 53.06, 50.08, 43.92, 42.52, 42.04, 36.43, 35.52, 35.44, 35.10, 33.22, 29.89, 23.04, 20.96, 11.29.

HRMS (**ESI**) m/z: calcd for $C_{19}H_{30}O_2N$ $[M+H]^+$ 304.2277, found 304.2289.

17β-acetamido-3-aza-A-homoandrost-4α-en-4-one (2ak)[21]



Compound **2ak** was synthesized according to the modified general procedure 3.1 using progesterone on a 1.0 mmol scale with 2.0 equiv. of hydroxylamine hydrochloride. The crude product was purified by silica gel column chromatography.

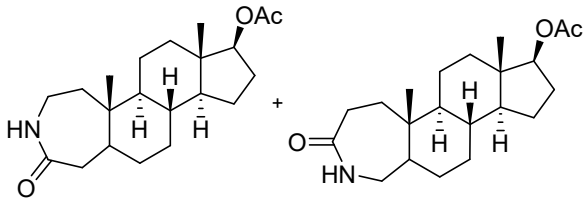
(R_f = 0.16; 10% methanol/DCM); yield: 75%, 258 mg; white solid; m.p. 276-278 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.78 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 5.50 (s, 1H), 3.66 (q, *J* = 9.1 Hz, 1H), 2.99 (s, 2H), 2.43 (td, *J* = 13.3, 4.1 Hz, 1H), 2.04 (d, *J* = 12.7 Hz, 1H), 1.89 – 1.76 (m, 6H), 1.69 – 1.26 (m, 7H), 1.24 – 1.15 (m, 2H), 1.07 (s, 3H), 1.04 – 0.90 (m, 3H), 0.64 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 168.95, 168.18, 159.33, 119.41, 58.18, 52.93, 51.71, 43.93, 42.83, 42.01, 36.87, 35.54, 35.47, 35.17, 33.24, 27.18, 23.15, 22.74, 20.96, 12.12.

HRMS (**ESI**) m/z: calcd for $C_{21}H_{33}O_2N_2$ $[M+H]^+$ 345.2542, found 345.2547.

17β-Acetoxy-3-aza-A-homoandrostan-4-one ($2al_1$) and 17β-Acetoxy-4-aza-A-homoandrostan-3-one($2al_2$)[22]



Compound **$2al_1$** and **$2al_2$** were obtained as a mixture (1:1). Synthesis was achieved according to the general procedure 3.1 using stanolone acetate on a 1.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.43; 5% methanol/DCM); Non-separable regioisomers; yield: 64%, 223 mg; white solid; m.p. 309-311 °C.

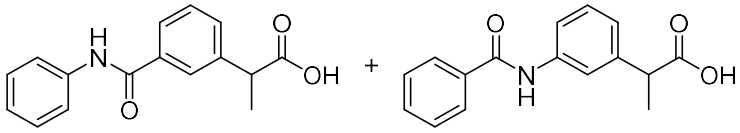
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.33 (s, 1H), 6.18 (s, 1H), 4.59 – 4.54 (m, 2H), 3.41 – 3.31 (m, 2H), 3.04 – 2.93 (m, 1H), 2.74 (d, *J* = 11.1 Hz, 1H), 2.61 – 2.49 (m, 2H), 2.37 – 2.05 (m, 4H), 2.02 (s, 6H), 1.91 – 1.78 (m, 4H), 1.76 – 1.56 (m, 9H), 1.53 – 1.43 (m, 4H), 1.38 – 1.28 (m, 8H), 1.26 – 1.22 (m, 4H), 1.19 – 1.10 (m, 3H), 1.02 (s, 2H), 0.91 (s, 6H), 0.77 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.80, 178.64, 171.30, 82.81, 54.11, 53.83, 50.81, 49.67, 44.57, 43.34, 42.47, 42.10, 39.70, 39.00, 38.83, 37.96, 37.02, 36.96, 35.36, 34.95, 34.59, 31.63, 31.46, 31.33, 30.95, 27.65, 23.56, 21.30, 20.88, 20.62, 12.20, 12.17, 12.08.

HRMS (**ESI**) m/z: calcd for $C_{21}H_{34}O_3N$ $[M+H]^+$ 348.2539, found 348.2542.

2-(3-(phenylcarbamoyl)phenyl)propanoic acid ($2am_1$) and

2-(3-benzamidophenyl)propanoic acid ($2am_2$)



Compound **$2am_1$** and **$2am_2$** were obtained as a mixture (1:1). Synthesis was achieved according to the general procedure 3.1 using ketoprofen on a 1.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.32; 5% methanol/DCM); Non-separable regioisomers; yield: 73%, 197 mg; light yellow thick liquid.

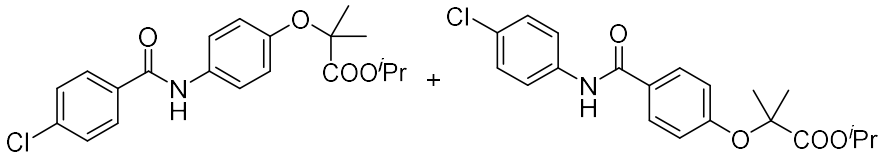
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 7.2 Hz, 2H), 7.79 (s, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.64 – 7.53 (m, 4H), 7.53 – 7.27 (m, 8H), 7.16 – 7.05 (m, 2H), 3.83 – 3.66 (m, 2H), 1.52 – 1.48 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 179.74, 179.31, 166.29, 166.19, 140.90, 140.70, 138.27, 137.93, 135.43, 134.77, 132.01, 131.19, 129.46, 129.13, 128.83, 127.24, 126.75, 126.17, 124.80, 123.99, 120.66, 119.79, 119.70, 45.34, 45.30, 18.19.

HRMS (**ESI**) m/z: calcd for $C_{16}H_{15}O_3NK$ $[M+K]^+$ 308.0689, found 308.0691.

isopropyl 2-(4-(4-chlorobenzamido)phenoxy)-2-methylpropanoate ($2an_1$) and

isopropyl 2-(4-((4-chlorophenyl)carbamoyl)phenoxy)-2-methylpropanoate ($2an_2$)



Compound **$2an_1$** and **$2an_2$** were obtained as a mixture (~10:1). Synthesis was achieved according to the general procedure 3.1 using fenofibrate on a 1.0 mmol scale. The crude product was purified by silica gel column chromatography.

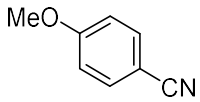
(R_f = 0.40; 20% EtOAc/hexanes); Non-separable regioisomers; Major isomer (**$2an_1$**); yield: 69%, 259 mg; white solid; m.p. 109-111 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 10.23 (s, 1H), 7.96 (d, *J* = 8.5 Hz, 2H), 7.61 (dd, *J* = 16.7, 8.7 Hz, 4H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.97 (hep, *J* = 6.2 Hz, 1H), 1.50 (s, 6H), 1.18 (d, *J* = 6.2 Hz, 6H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 172.70, 164.10, 151.21, 136.29, 133.67, 133.38, 129.54, 128.45, 121.54, 119.16, 78.88, 68.52, 25.01, 21.31.

HRMS (**ESI**) m/z: calcd for $C_{20}H_{22}O_4NClNa$ $[M+Na]^+$ 398.1135, found 398.1133.

4-methoxybenzonitrile (4a)[7]



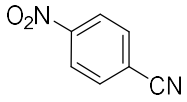
Compound **4a** was synthesized according to the general procedure 3.2 using 4-methoxybenzaldehyde on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.50; 10% EtOAc/hexanes); yield: 92%, 245 mg; light yellow solid; m.p. 60-62 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.79 – 7.76 (m, 2H), 7.13 – 7.09 (m, 2H), 3.85 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 162.72, 134.20, 119.18, 115.14, 102.81, 55.70.

4-nitrobenzonitrile (4b)[23]



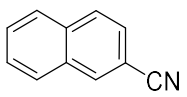
Compound **4b** was synthesized according to the general procedure 3.2 using 4-nitrobenzaldehyde on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.40; 10% EtOAc/hexanes); yield: 67%, 199 mg; white solid; m.p. 146-148 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.8 Hz, 2H), 7.90 (d, *J* = 8.8 Hz, 2H).

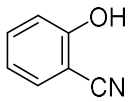
^{13}C NMR (101 MHz, $CDCl_3$): δ 150.17, 133.61, 124.43, 118.47, 116.92.

2-naphthonitrile (4c)[24]



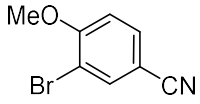
Compound **4c** was synthesized according to the general procedure 3.2 using 2-naphthaldehyde on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.
(R_f = 0.45; 05% EtOAc/hexanes); yield: 73%, 224 mg; off white solid; m.p. 65-67 °C.
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 7.91 (t, *J* = 8.8 Hz, 3H), 7.65 – 7.58 (m, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 134.78, 134.29, 132.39, 129.33, 129.17, 128.54, 128.18, 127.79, 126.48, 119.38, 109.52.

2-hydroxybenzonitrile (4d)[25]



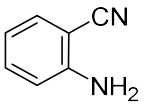
Compound **4d** was synthesized according to the general procedure 3.2 using 2-hydroxybenzaldehyde on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.
(R_f = 0.42; 10% EtOAc/hexanes); yield: 75%, 178 mg; white solid; m.p. 96-98 °C.
^{1}H NMR (400 MHz, DMSO-d_6): δ 11.06 (s, 1H), 7.59 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.50 –7.46 (m, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.94 – 6.90 (m, 1H).
^{13}C NMR (101 MHz, DMSO-d_6): 160.15, 134.75, 133.27, 119.59, 117.05, 116.17, 98.85.

3-bromo-4-methoxybenzonitrile (4e)[26]



Compound **4e** was synthesized according to the general procedure 3.2 using 3-bromo 4-methoxybenzaldehyde on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.
(R_f = 0.37; 10% EtOAc/hexanes); yield: 87%, 369 mg; white solid; m.p. 120-122 °C.
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 2.0 Hz, 1H), 7.60 (dd, *J* = 8.6, 2.0 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 1H), 3.96 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$): δ 159.57, 136.83, 133.31, 117.90, 112.47, 112.03, 105.38, 56.71.

2-aminobenzonitrile (6a)[27]



Compound **6a** was synthesized according to the general procedure 3.2 using isatin on a 2.0 mmol scale. The crude product was purified by silica gel column chromatography.

(R_f = 0.65; 10% EtOAc/hexanes); yield: 73%, 323 mg; off white solid; m.p. 48-50 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.36 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.31 – 7.26 (m, 1H), 6.77 (dd, *J* = 8.4, 0.4 Hz, 1H), 6.59 – 6.55 (m, 1H), 6.02 (s, 2H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 151.62, 133.97, 132.45, 118.16, 115.90, 115.19, 93.41.

9. References

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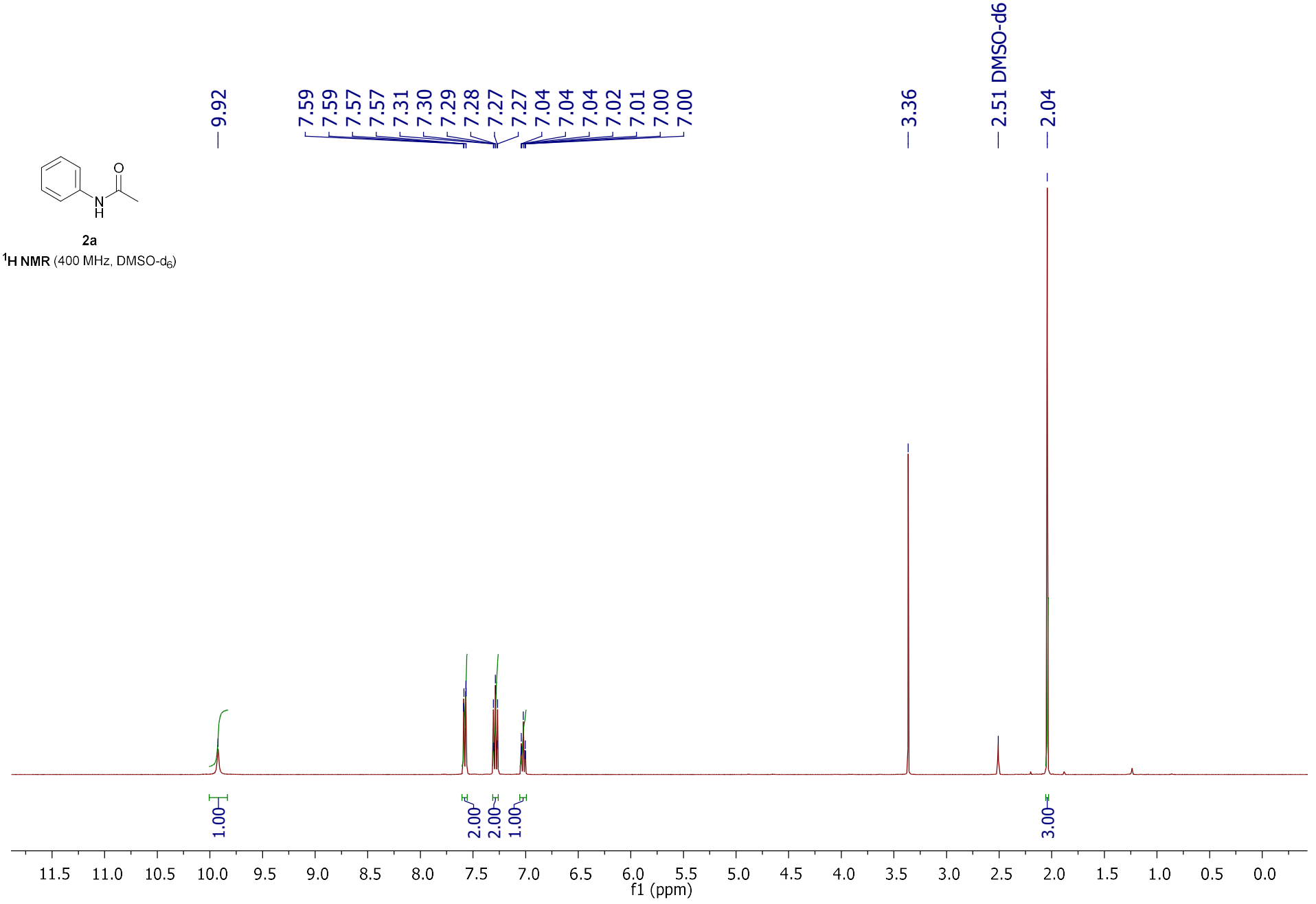
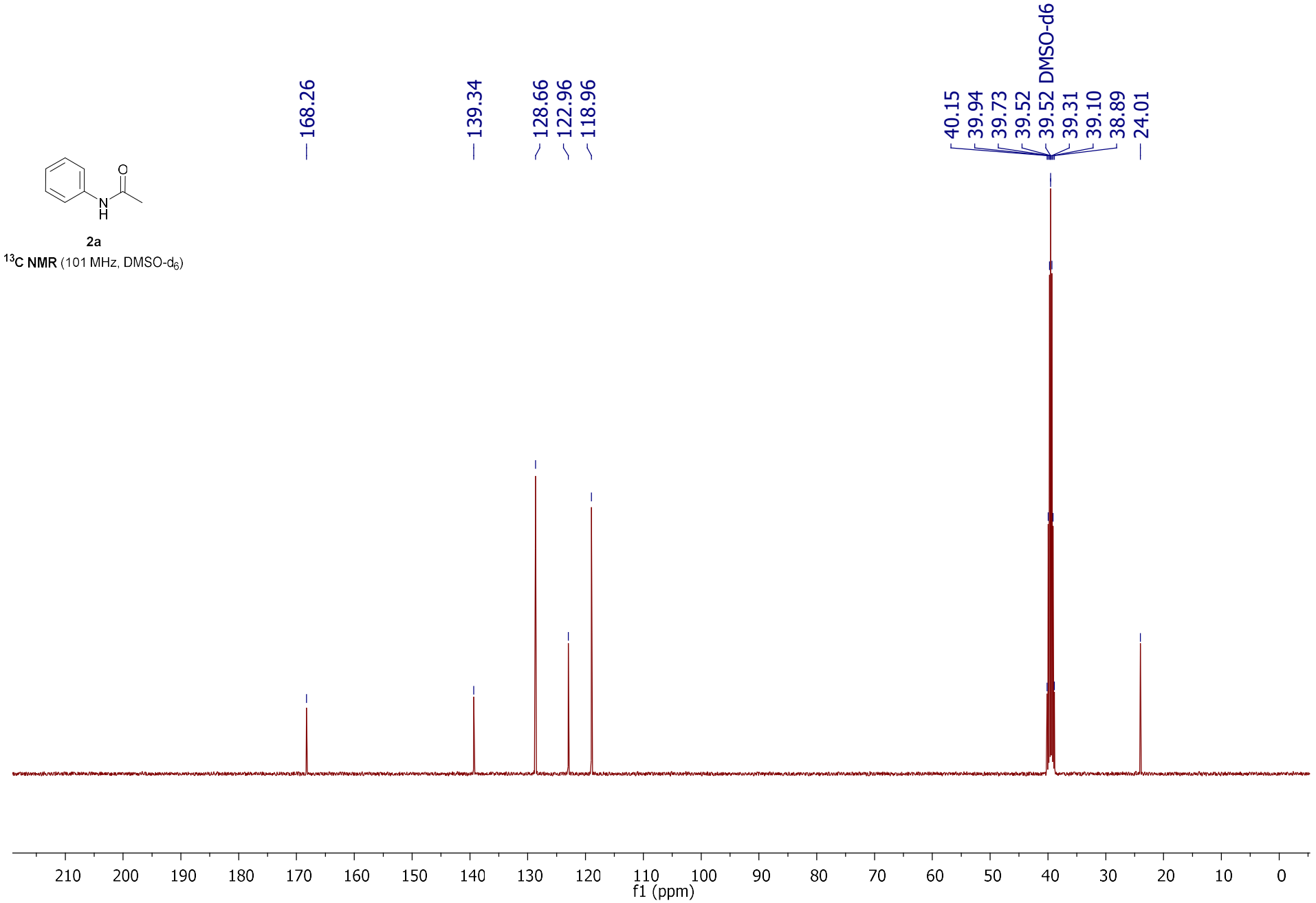
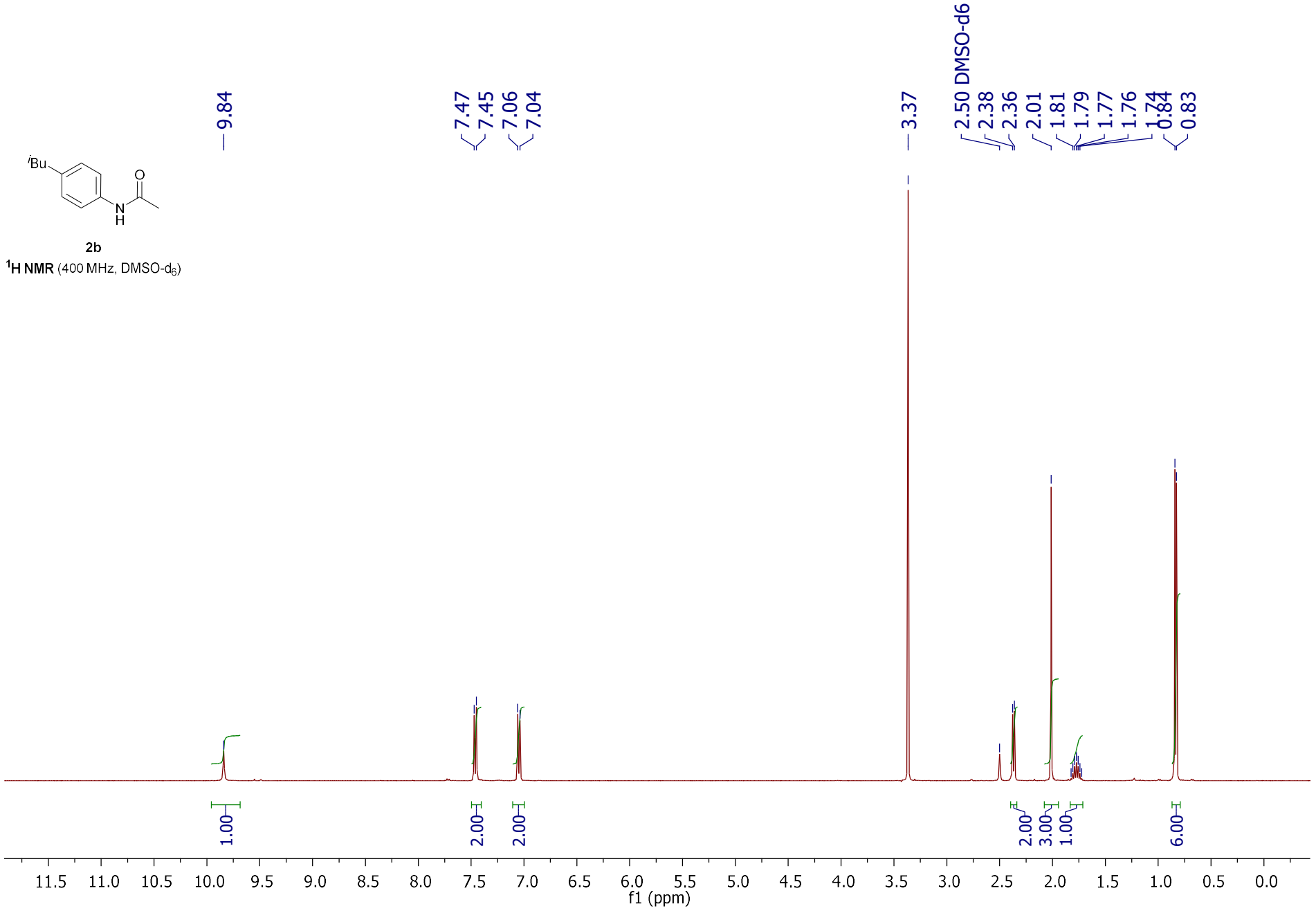
10. NMR Spectra



2a

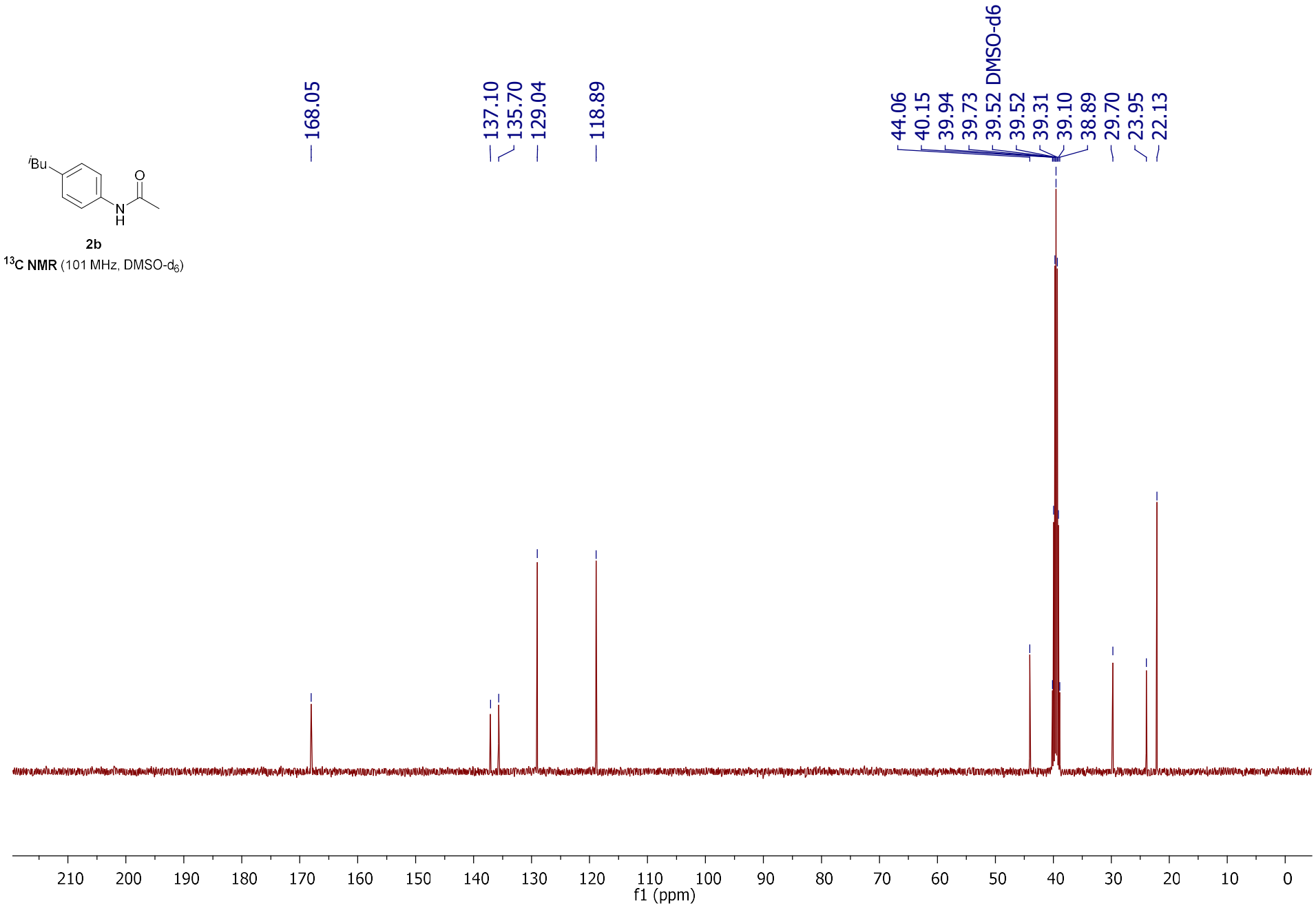
^{1}**H NMR** (400 MHz, DMSO-d_6)

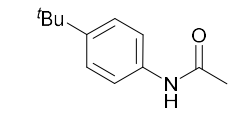

168.26
139.34
128.66
122.96
118.96
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
24.01
O
N
H
2a
13C NMR (101 MHz, DMSO-d6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



2b

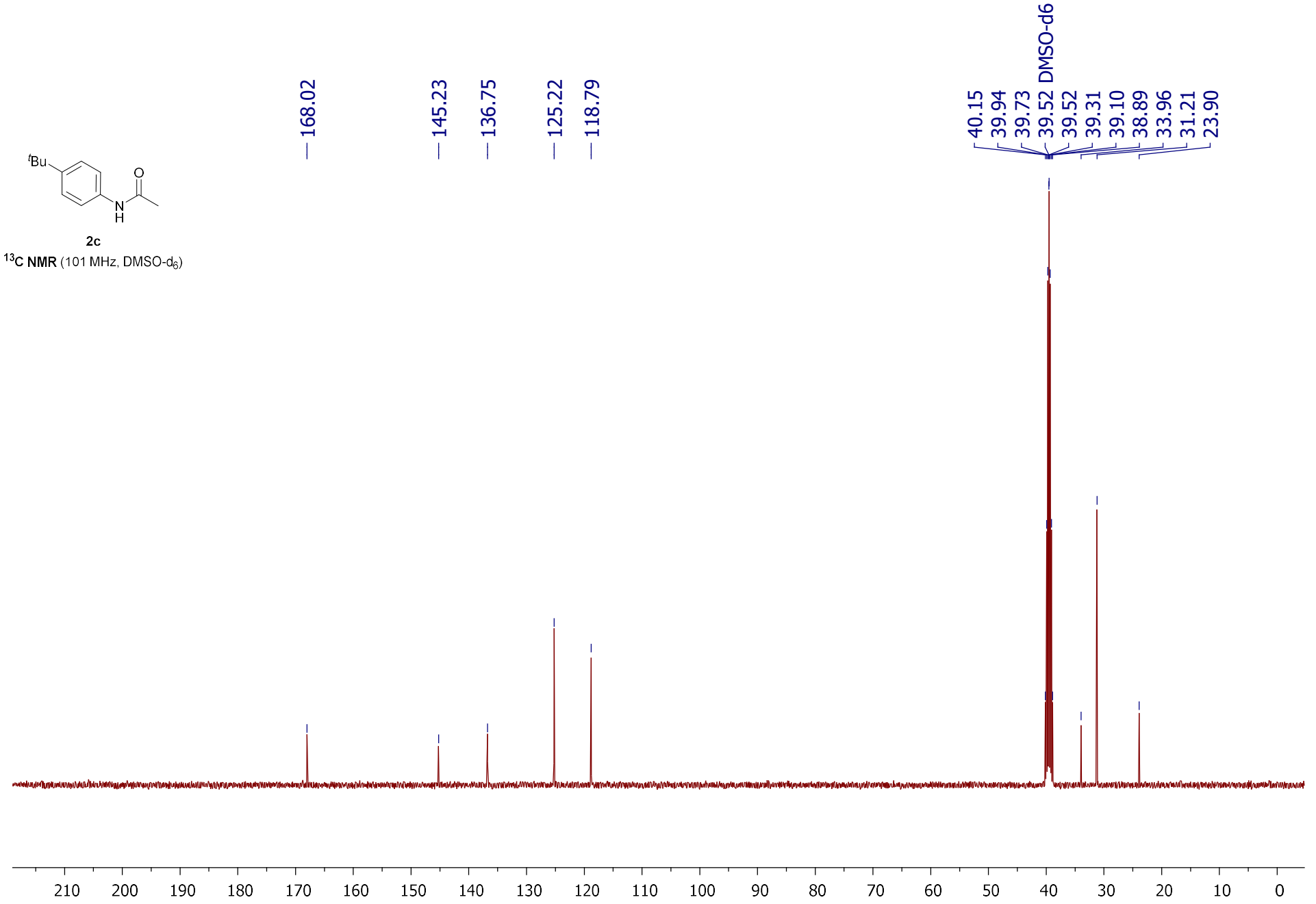
^{1}H NMR (400 MHz, DMSO-d_6)

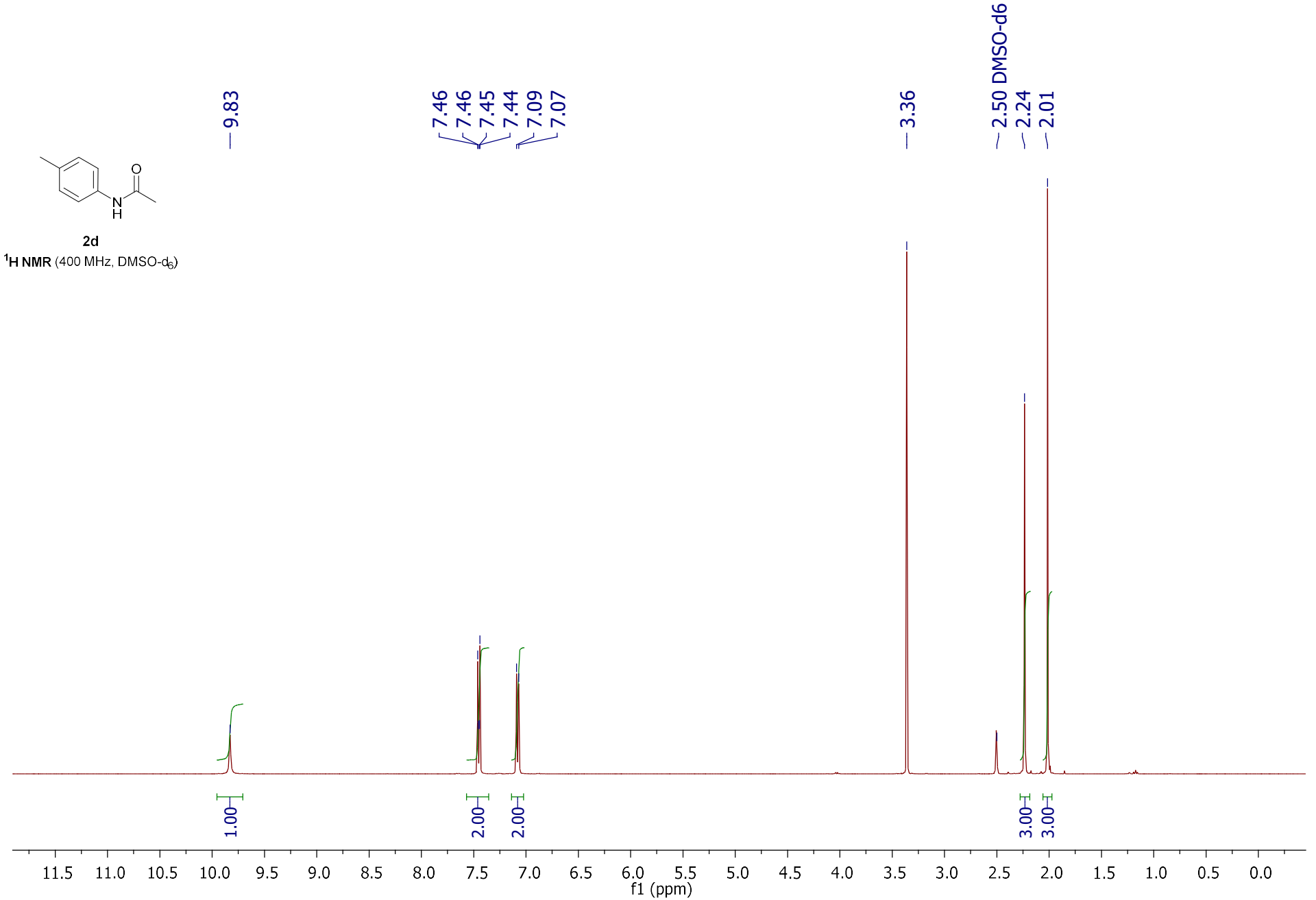

168.05
137.10
135.70
129.04
118.89
44.06
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
29.70
23.95
22.13
tBu
O
N
H
2b
13C NMR (101 MHz, DMSO-d6)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



2c

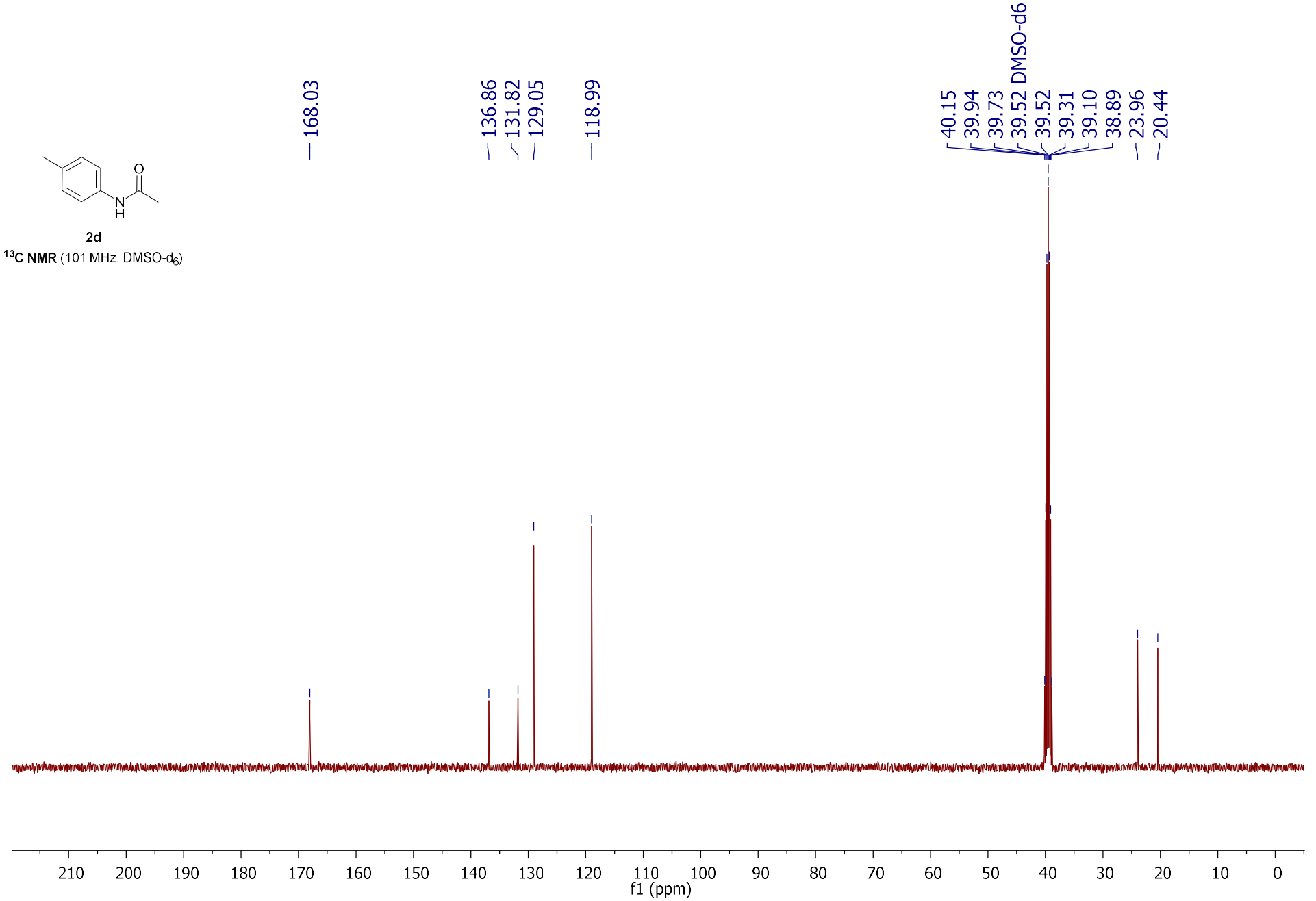
^{1}H NMR (400 MHz, DMSO-d_6)

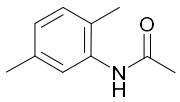

tBu
O
N
H
2c
13C NMR (101 MHz, DMSO-d6)
168.02
145.23
136.75
125.22
118.79
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
33.96
31.21
23.90
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



2d

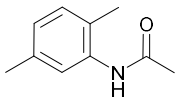
^{1}H NMR (400 MHz, DMSO-d_6)


168.03
136.86
131.82
129.05
118.99
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
23.96
20.44
O
N
H
2d
13C NMR (101 MHz, DMSO-d6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



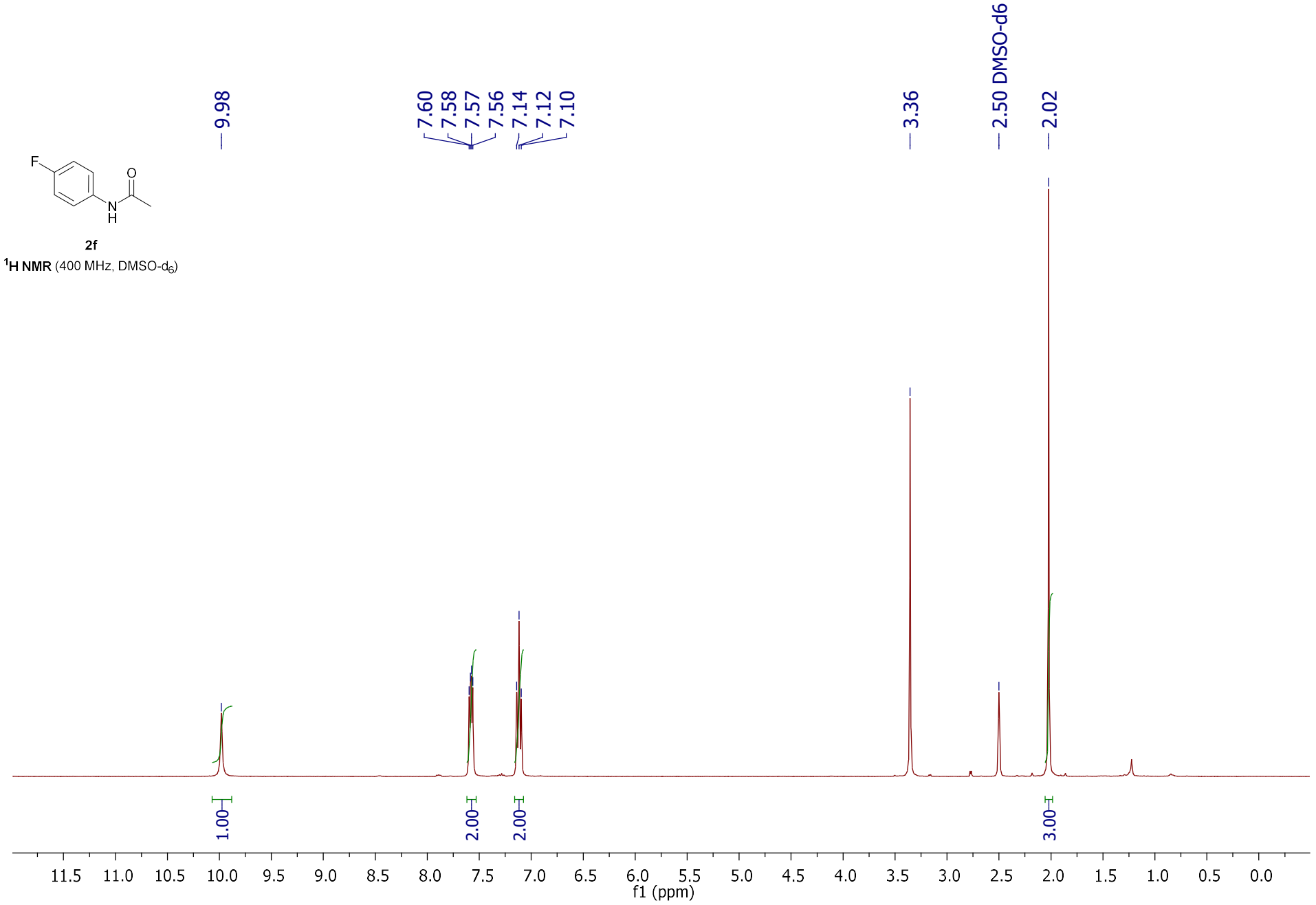
2e

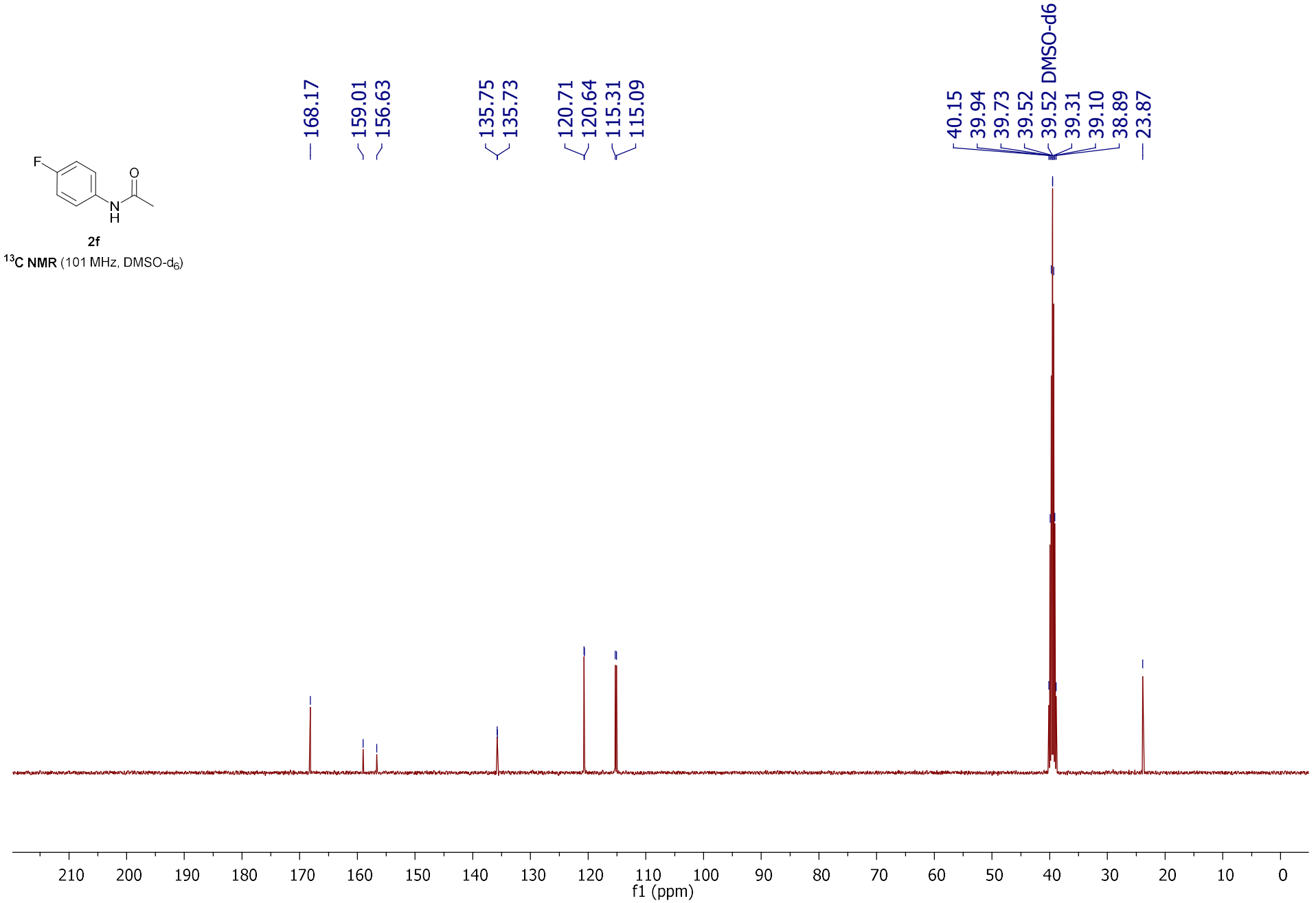
^{1}H NMR (400 MHz, DMSO-d_6)

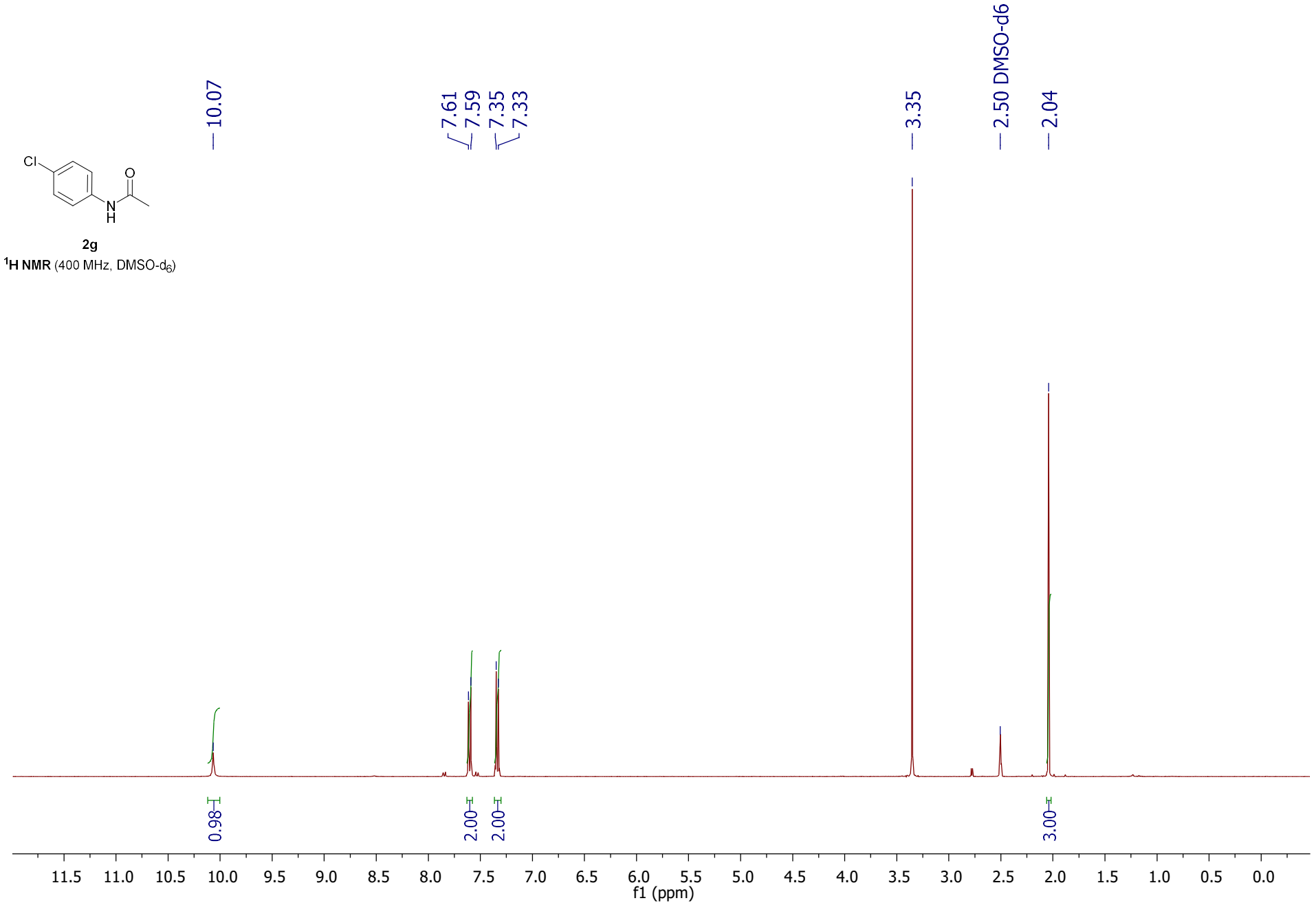


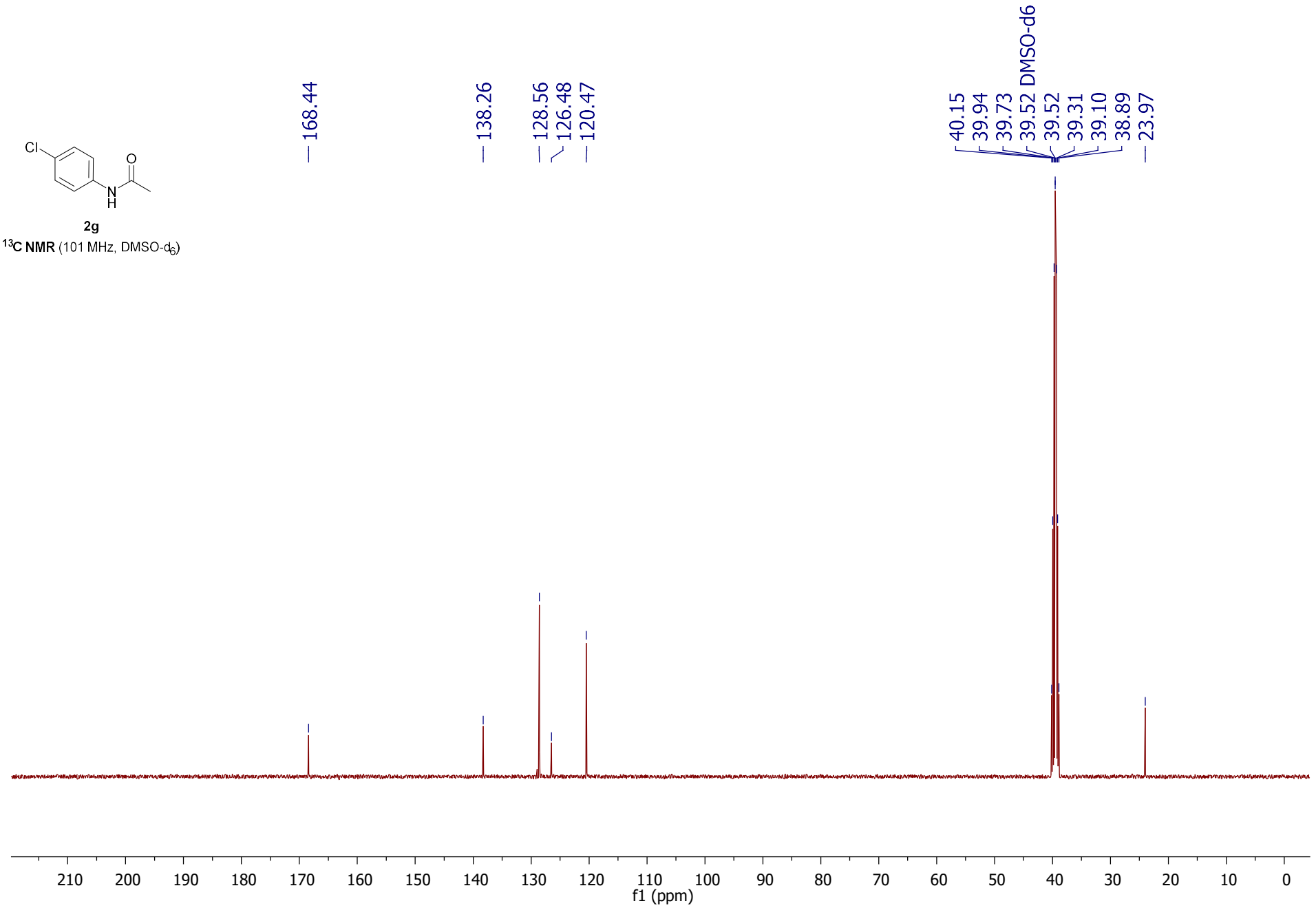
2e

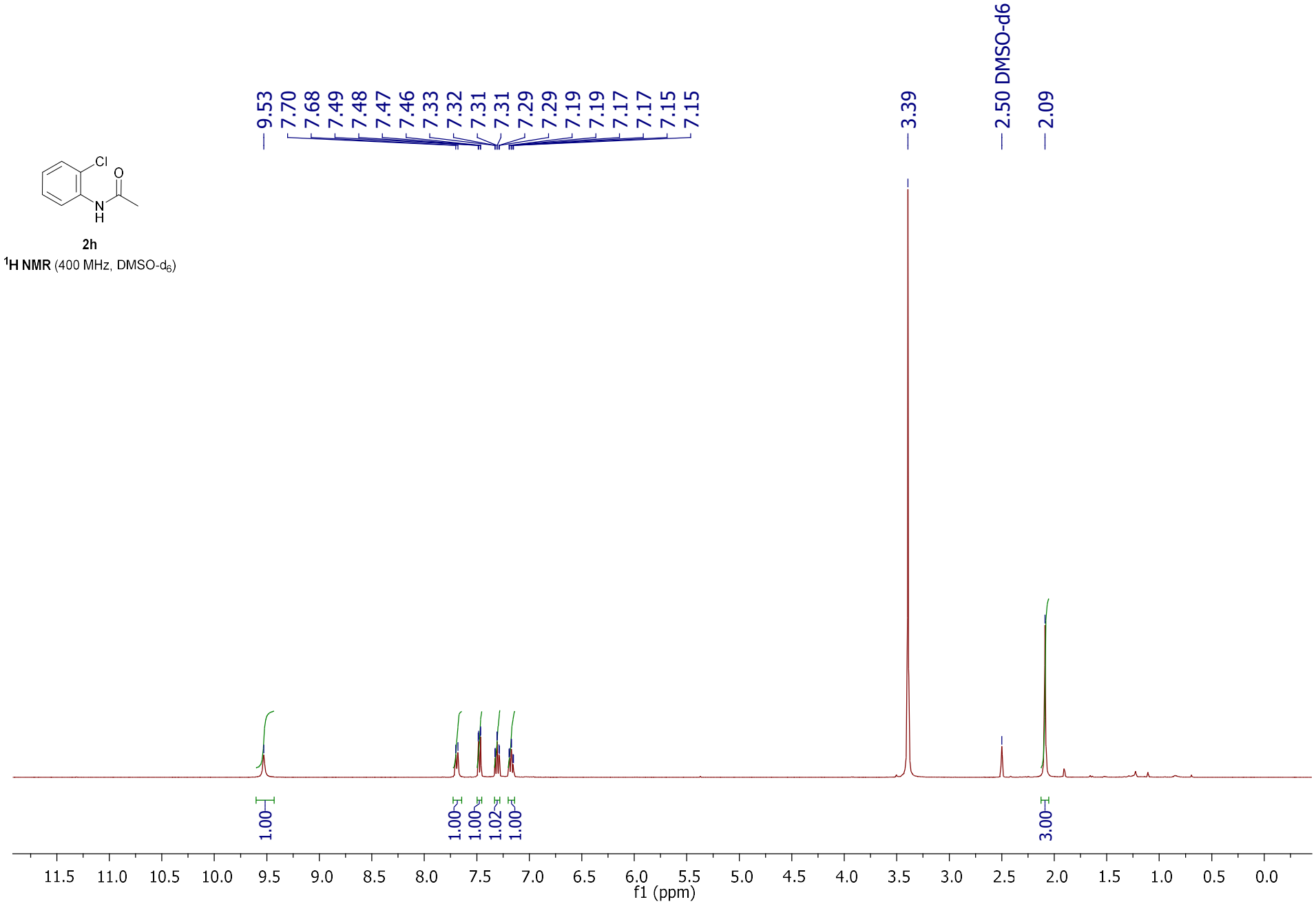
^{13}**C NMR** (101 MHz, DMSO-d_6)

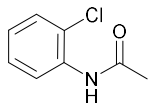

9.98
7.60
7.58
7.57
7.56
7.14
7.12
7.10
3.36
2.50 DMSO-d6
2.02
F
O
N
H
2f
1H NMR (400 MHz, DMSO-d6)
1.00
2.00
2.00
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


F
O
N
H
2f
13C NMR (101 MHz, DMSO-d6)
168.17
159.01
156.63
135.75
135.73
120.71
120.64
115.31
115.09
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
23.87
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.07
7.61
7.59
7.35
7.33
3.35
2.50 DMSO-d6
2.04
Cl
O
N
H
2g
1H NMR (400 MHz, DMSO-d6)
0.98
2.00
2.00
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

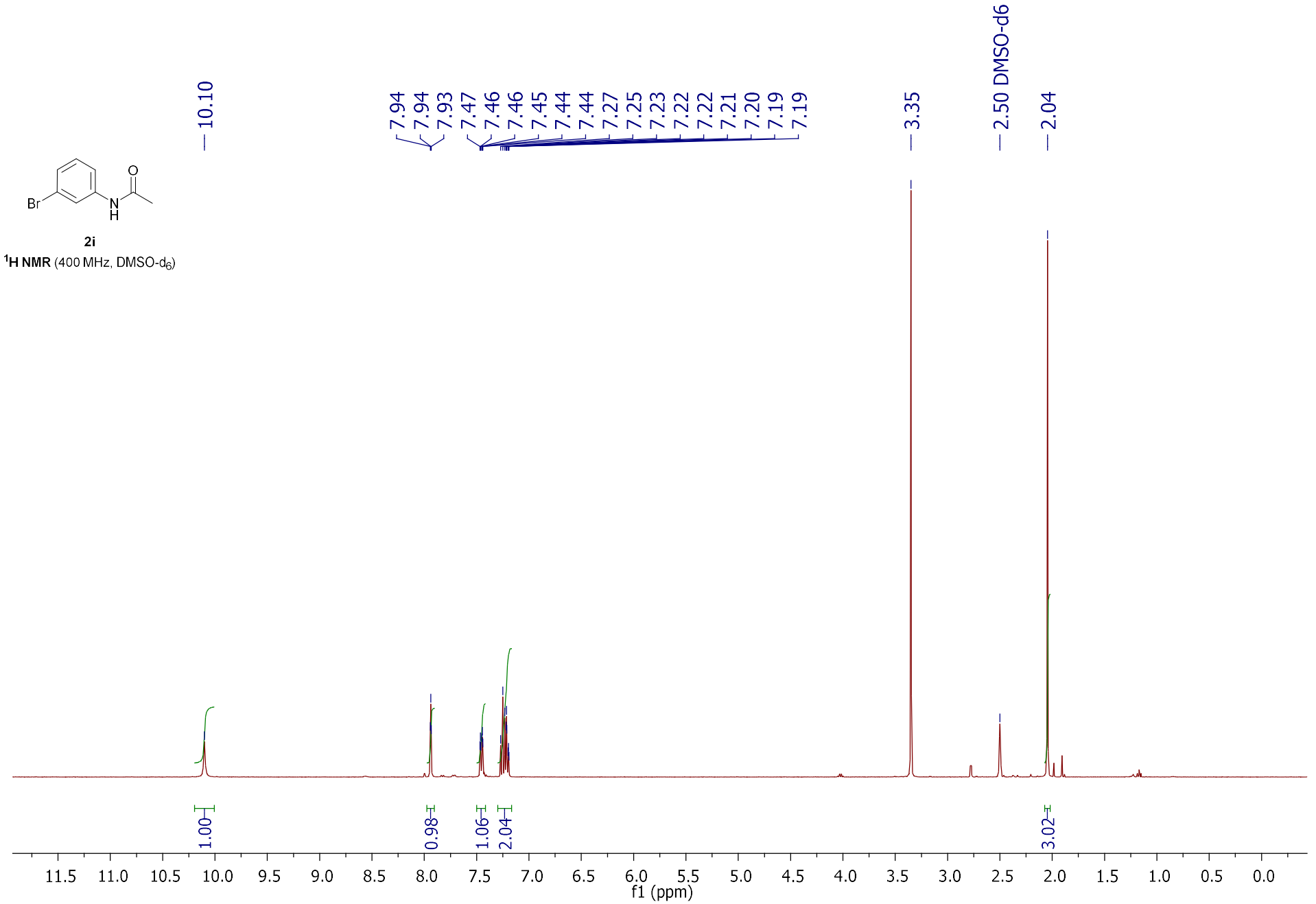

Cl
O
N
H
2g
13C NMR (101 MHz, DMSO-d6)
168.44
138.26
128.56
126.48
120.47
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
23.97
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

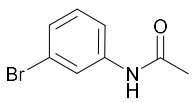

9.53
7.70
7.68
7.49
7.48
7.47
7.46
7.33
7.32
7.31
7.31
7.29
7.29
7.19
7.19
7.17
7.17
7.15
7.15
3.39
2.50 DMSO-d6
2.09
Cl
O
N
H
2h
1H NMR (400 MHz, DMSO-d6)
1.00
1.00
1.00
1.02
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



2h

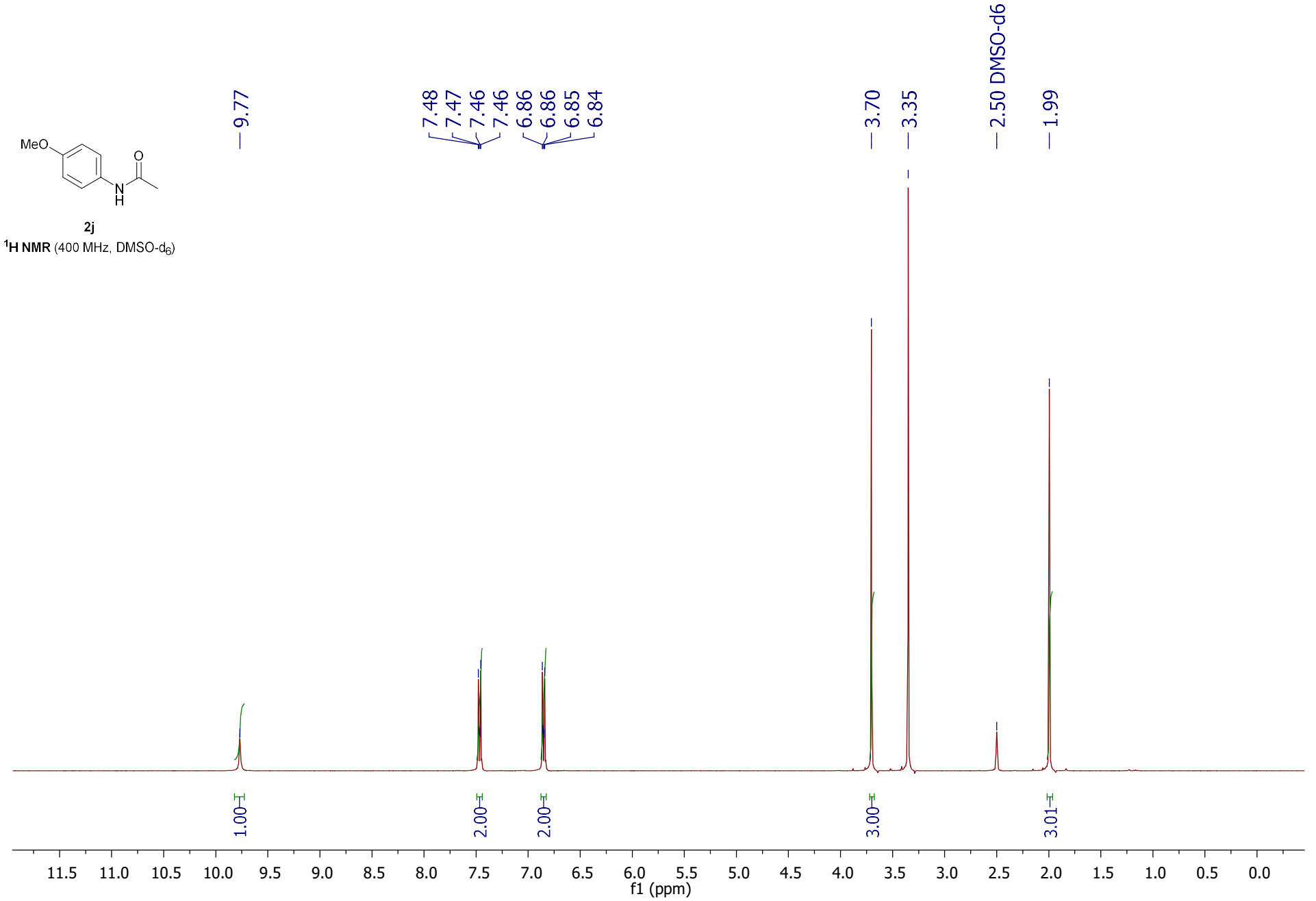
^{13}**C NMR** (101 MHz, DMSO-d_6)

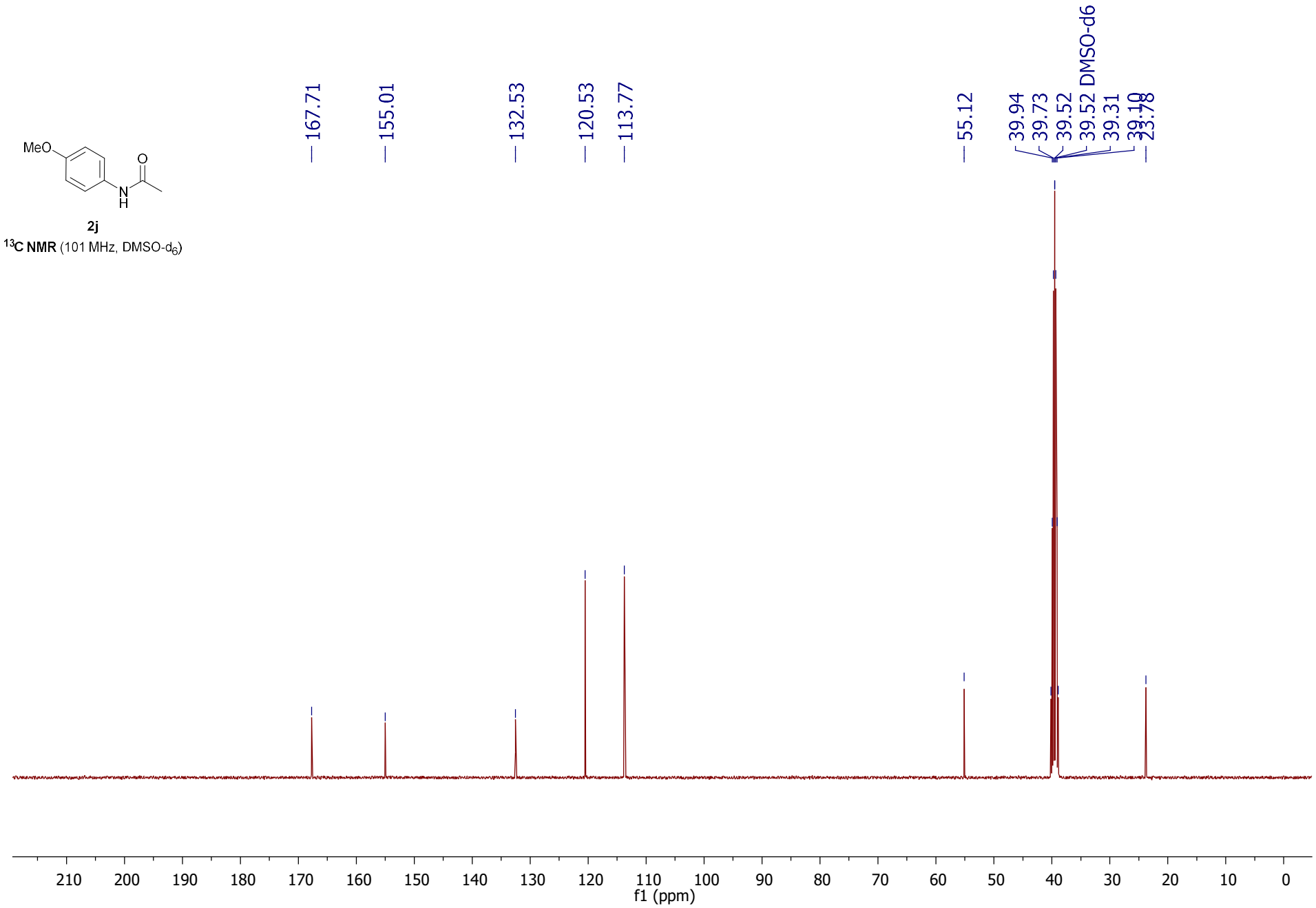

10.10
7.94
7.94
7.93
7.47
7.46
7.46
7.45
7.44
7.44
7.27
7.25
7.23
7.22
7.22
7.21
7.20
7.19
7.19
3.35
2.50 DMSO-d6
2.04
Br
N
H
O
2i
1H NMR (400 MHz, DMSO-d6)
1.00
0.98
1.06
2.04
3.02
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

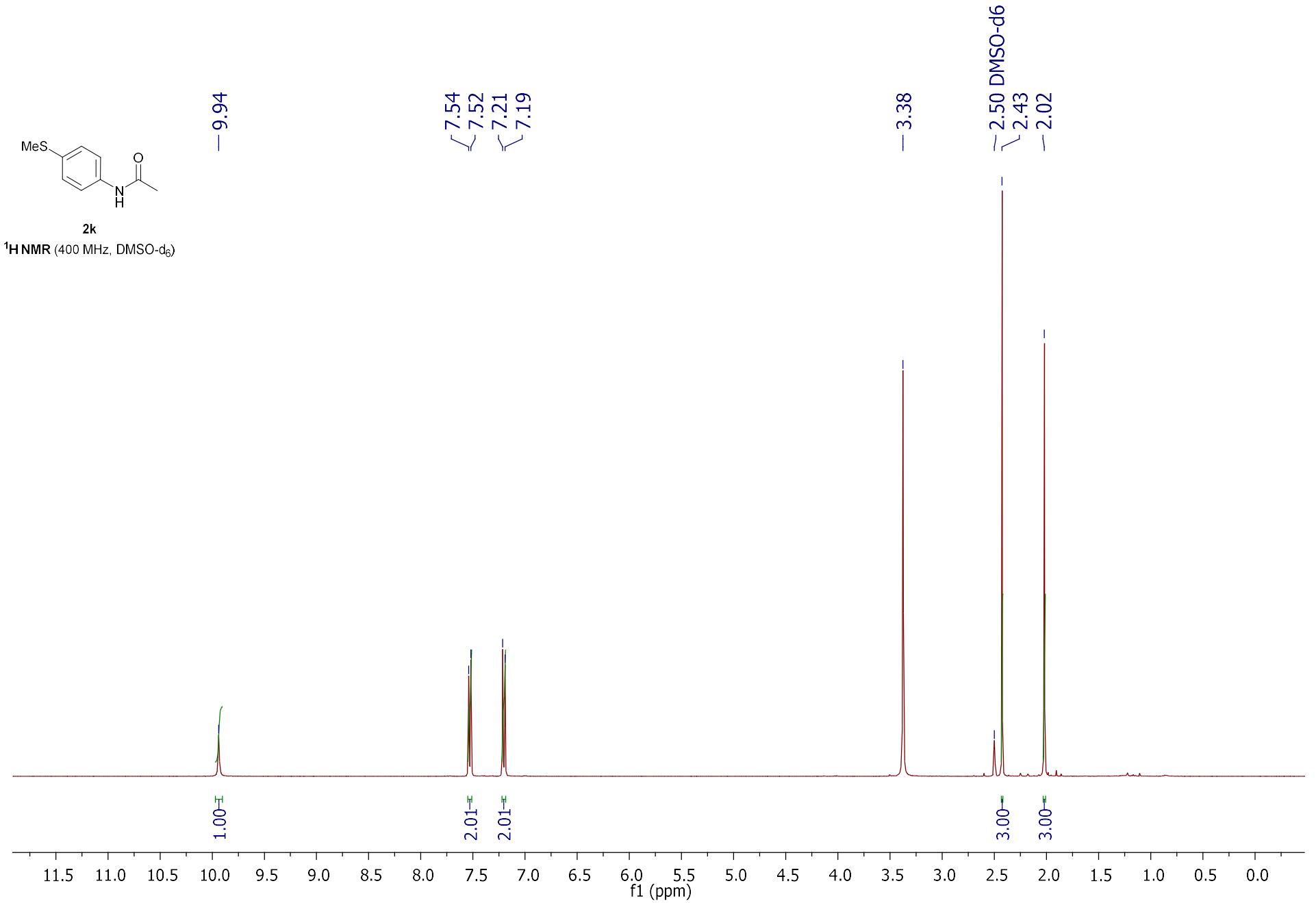


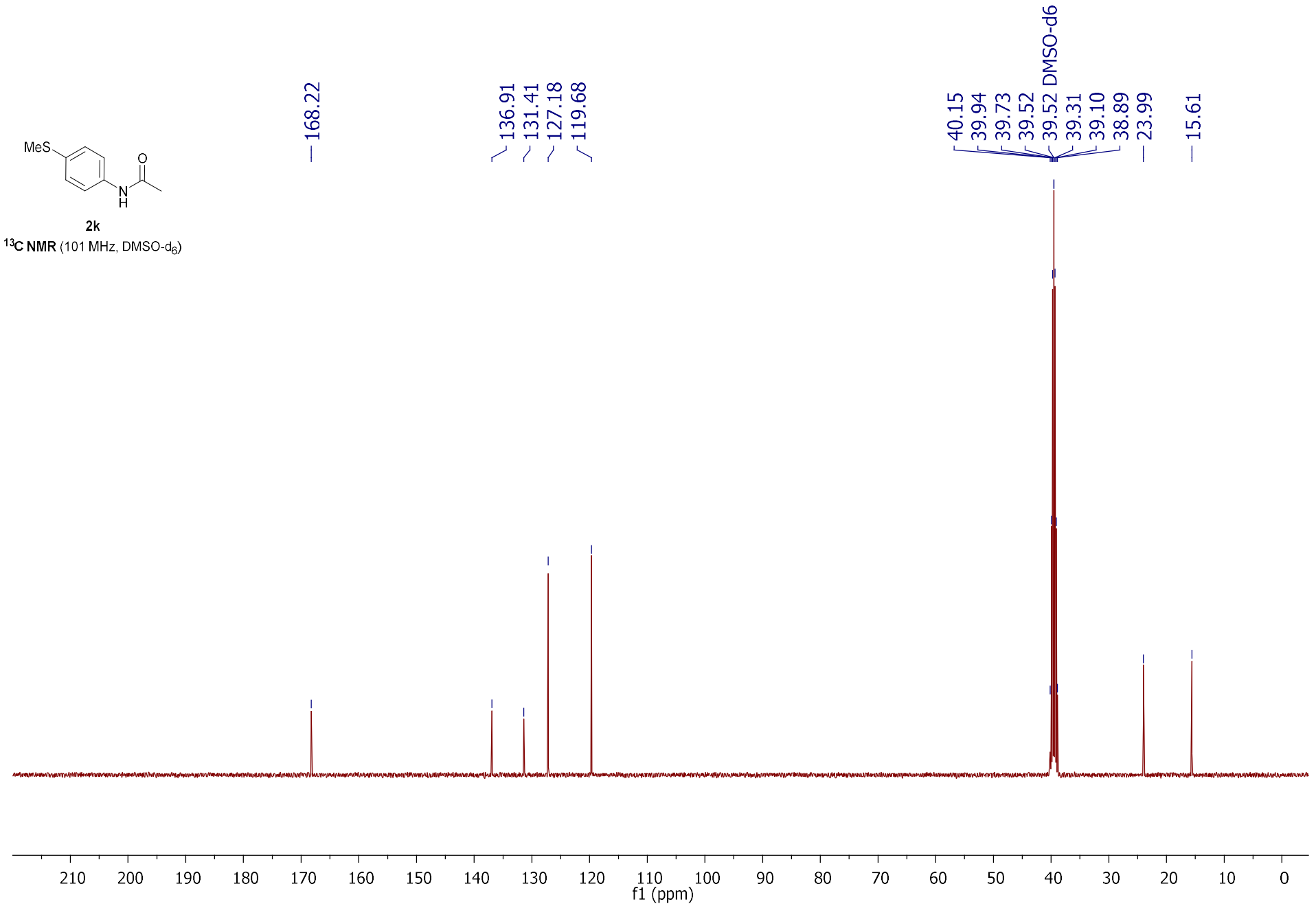
2i

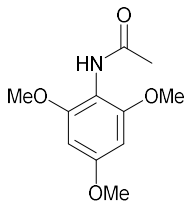
^{13}C NMR (101 MHz, DMSO-d_6)


MeO
O
N
H
2j
1H NMR (400 MHz, DMSO-d6)
9.77
7.48
7.47
7.46
7.46
6.86
6.86
6.85
6.84
3.70
3.35
2.50 DMSO-d6
1.99
1.00
2.00
2.00
3.00
3.01
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


MeO
O
N
H
2j
13C NMR (101 MHz, DMSO-d6)
167.71
155.01
132.53
120.53
113.77
55.12
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
23.78
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

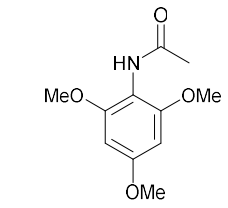

MeS
O
N
H
2k
1H NMR (400 MHz, DMSO-d6)
9.94
7.54
7.52
7.21
7.19
3.38
2.50 DMSO-d6
2.43
2.02
1.00
2.01
2.01
3.00
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


MeS
O
N
H
2k
13C NMR (101 MHz, DMSO-d6)
168.22
136.91
131.41
127.18
119.68
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
23.99
15.61
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



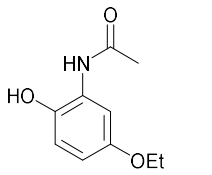
2l

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



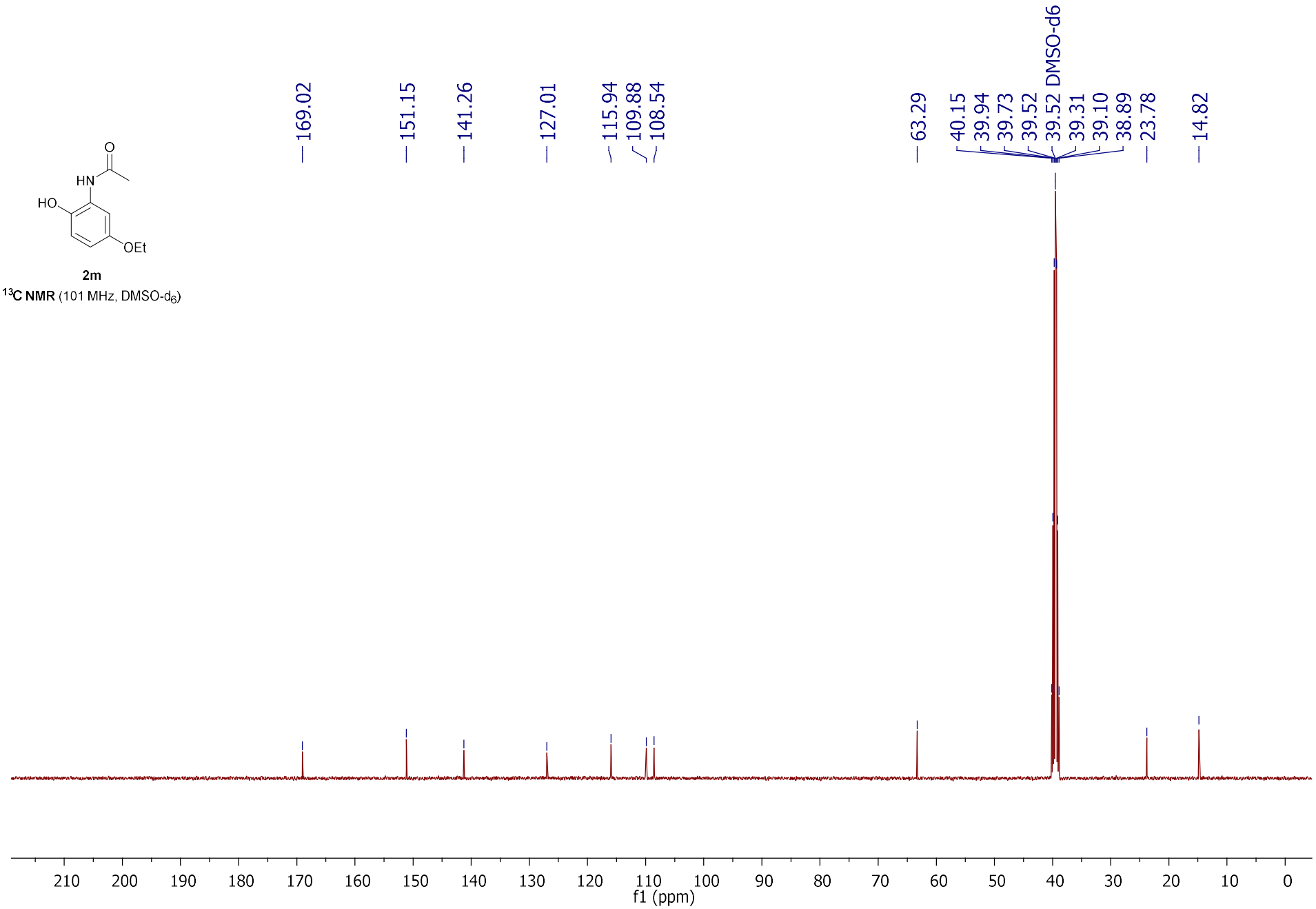
2l

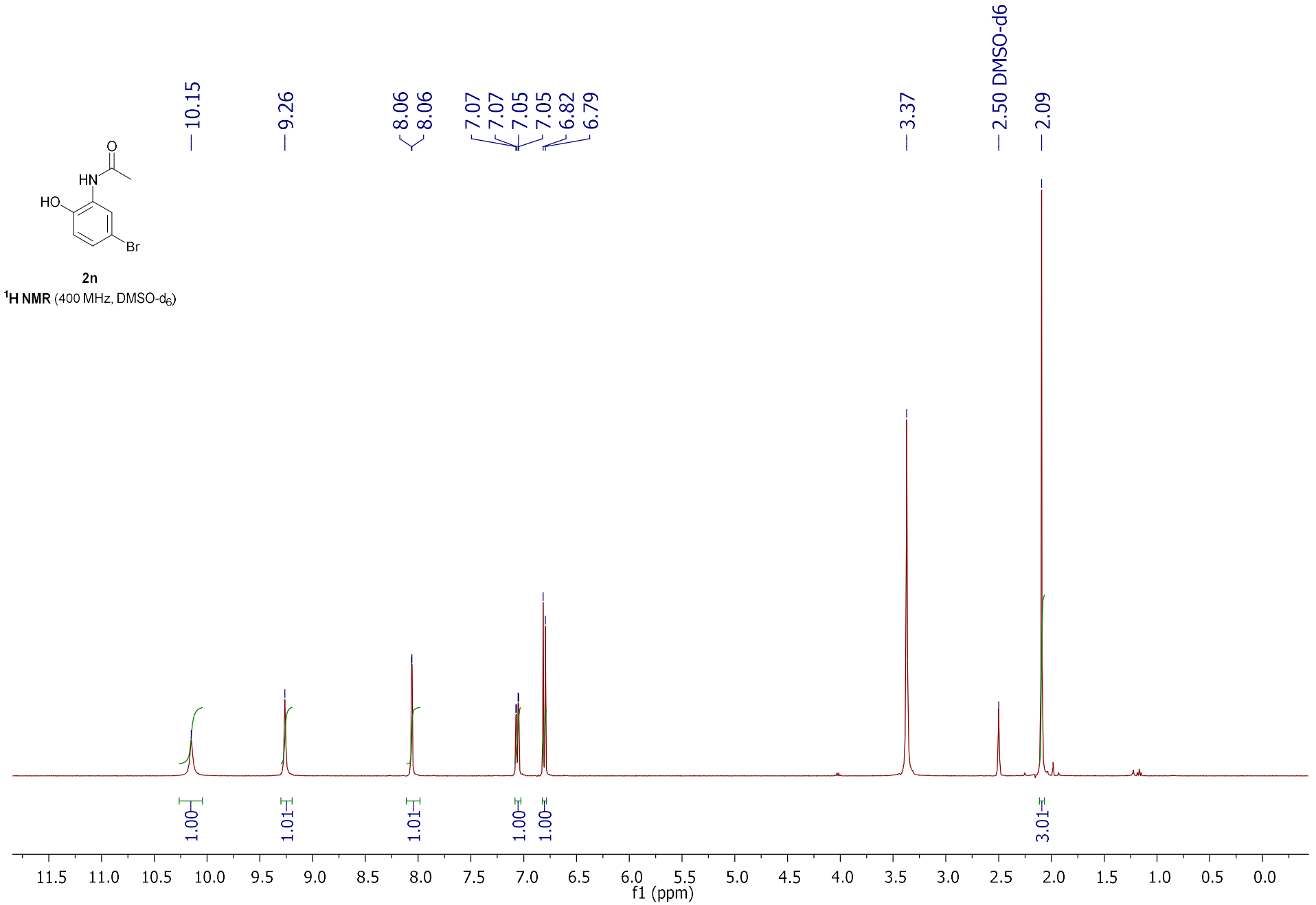
^{13}C NMR (101 MHz, DMSO-d_6)

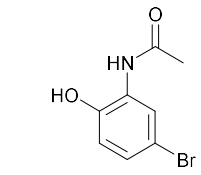


2m

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

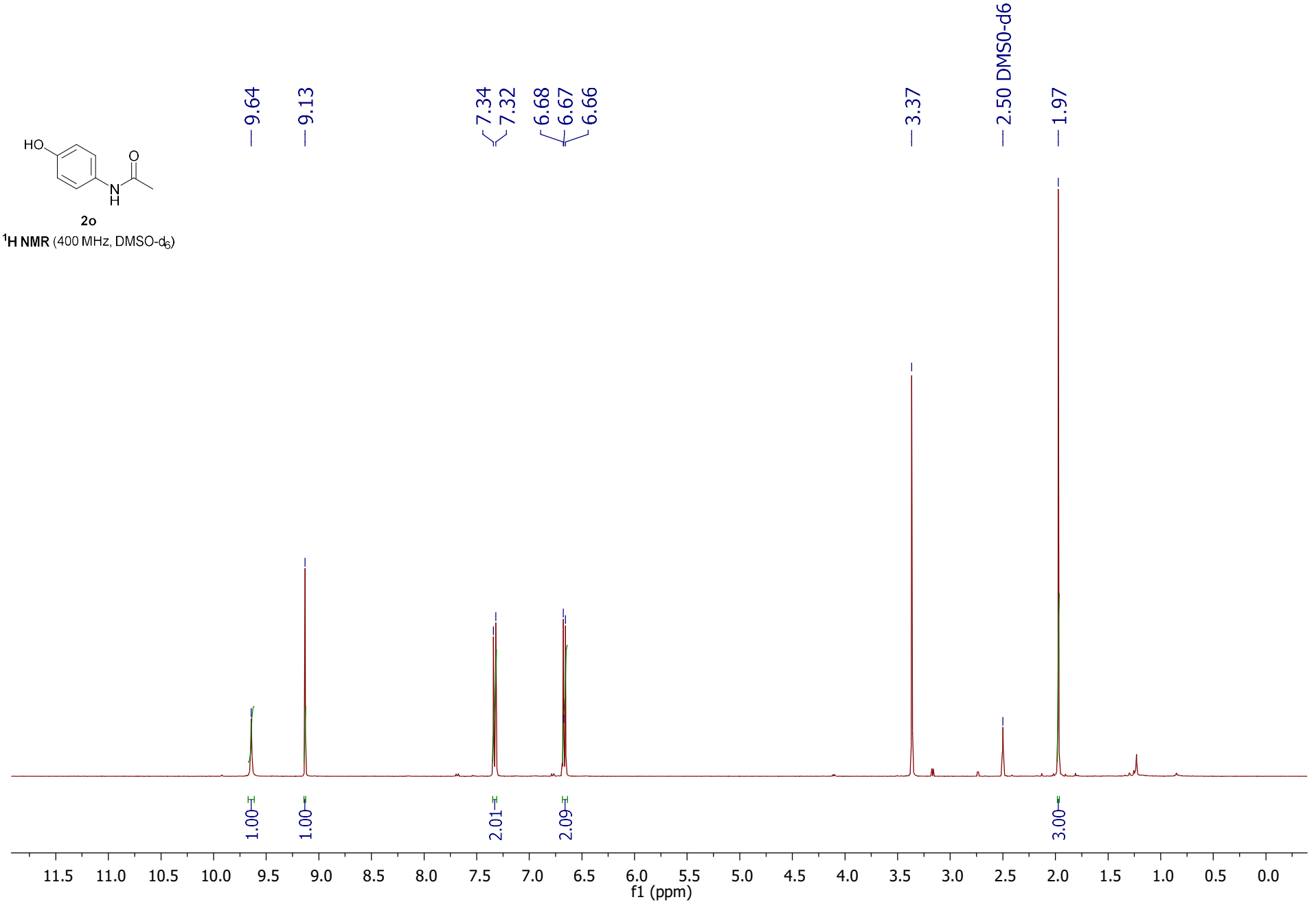

HN
O
HO
OEt
2m
13C NMR (101 MHz, DMSO-d6)
169.02
151.15
141.26
127.01
115.94
109.88
108.54
63.29
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
23.78
14.82
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

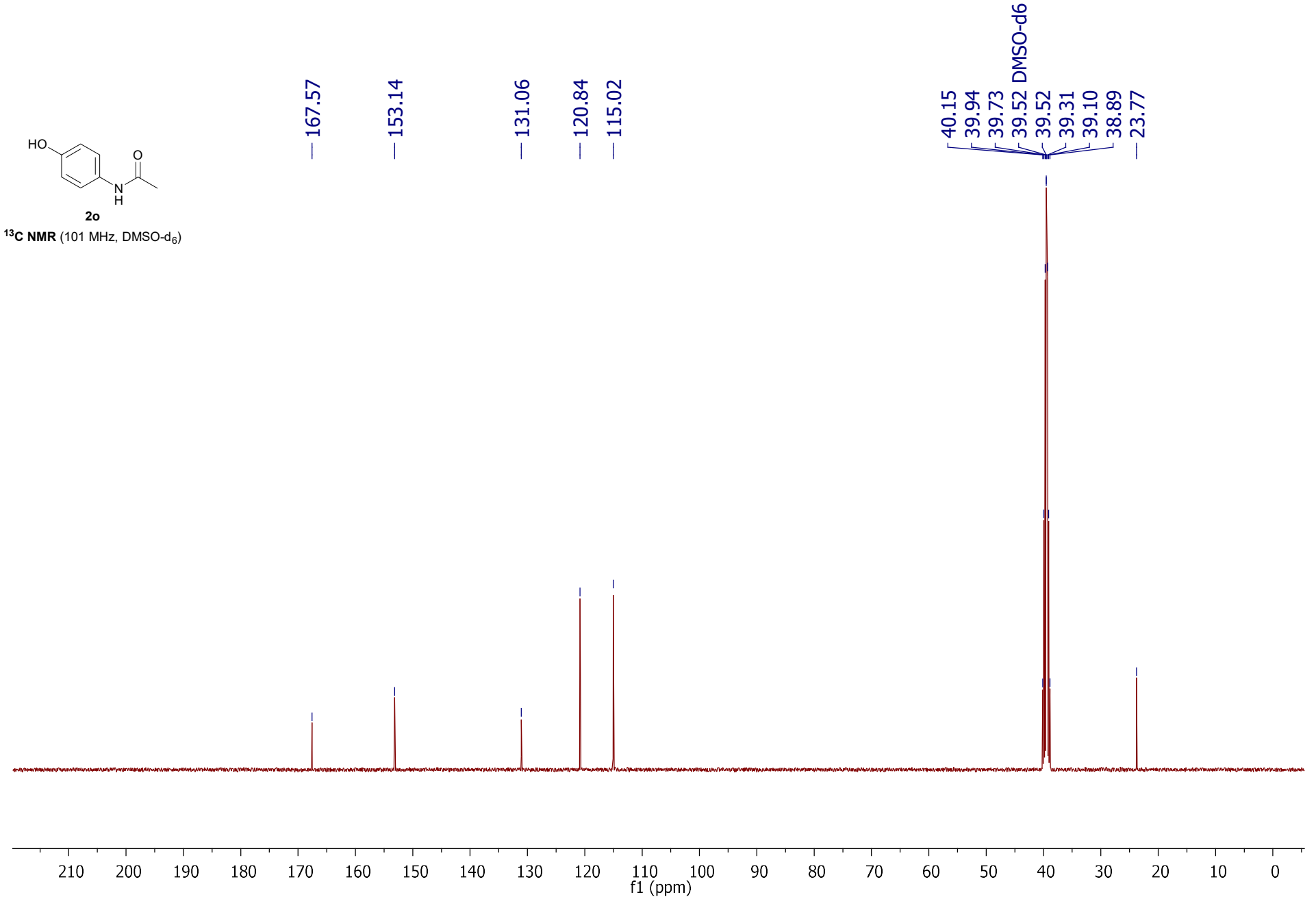

10.15
9.26
8.06
8.06
7.07
7.07
7.05
7.05
6.82
6.79
3.37
2.50 DMSO-d6
2.09
HO
HN
O
Br
2n
1H NMR (400 MHz, DMSO-d6)
1.00
1.01
1.01
1.00
1.00
3.01
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

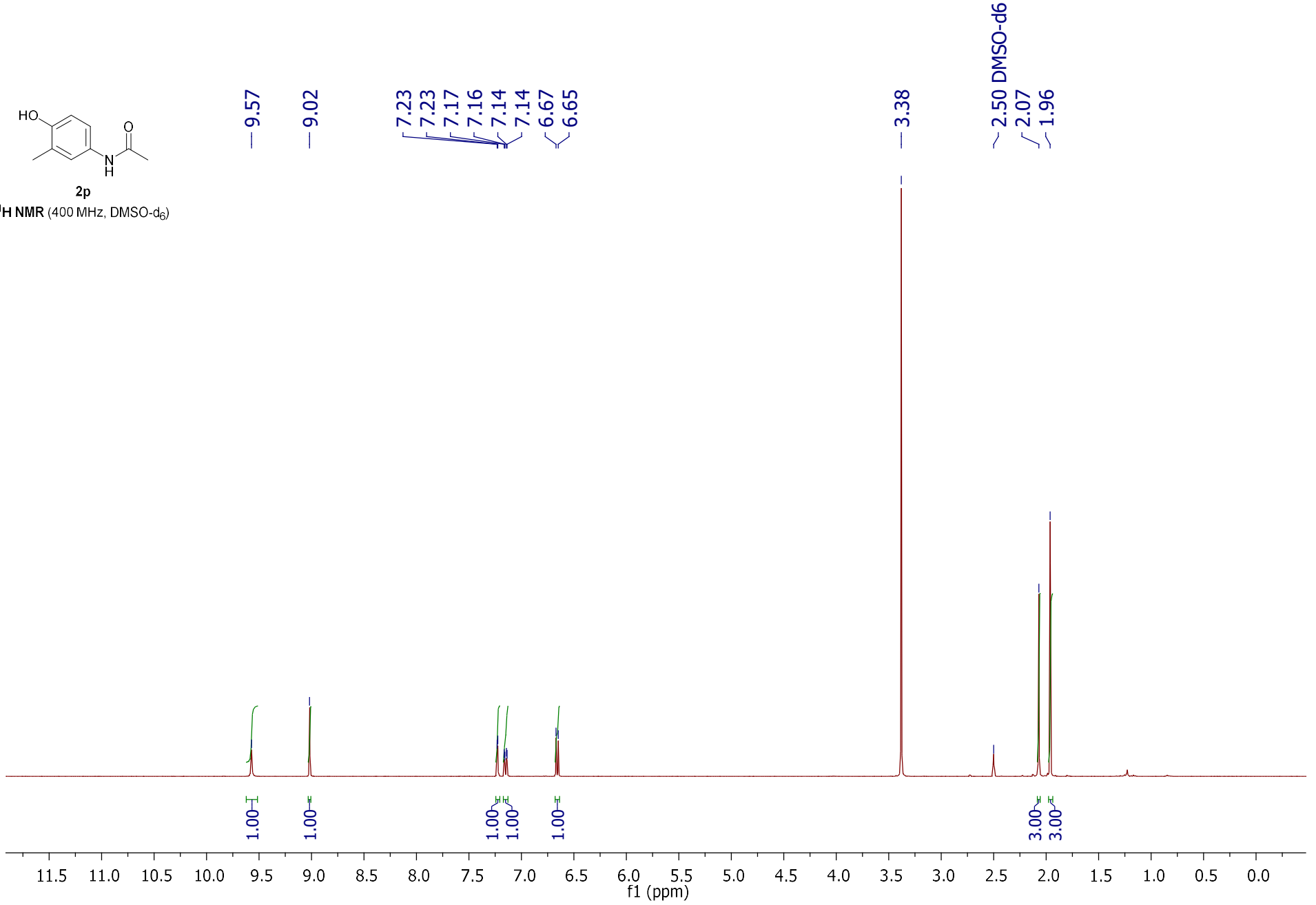


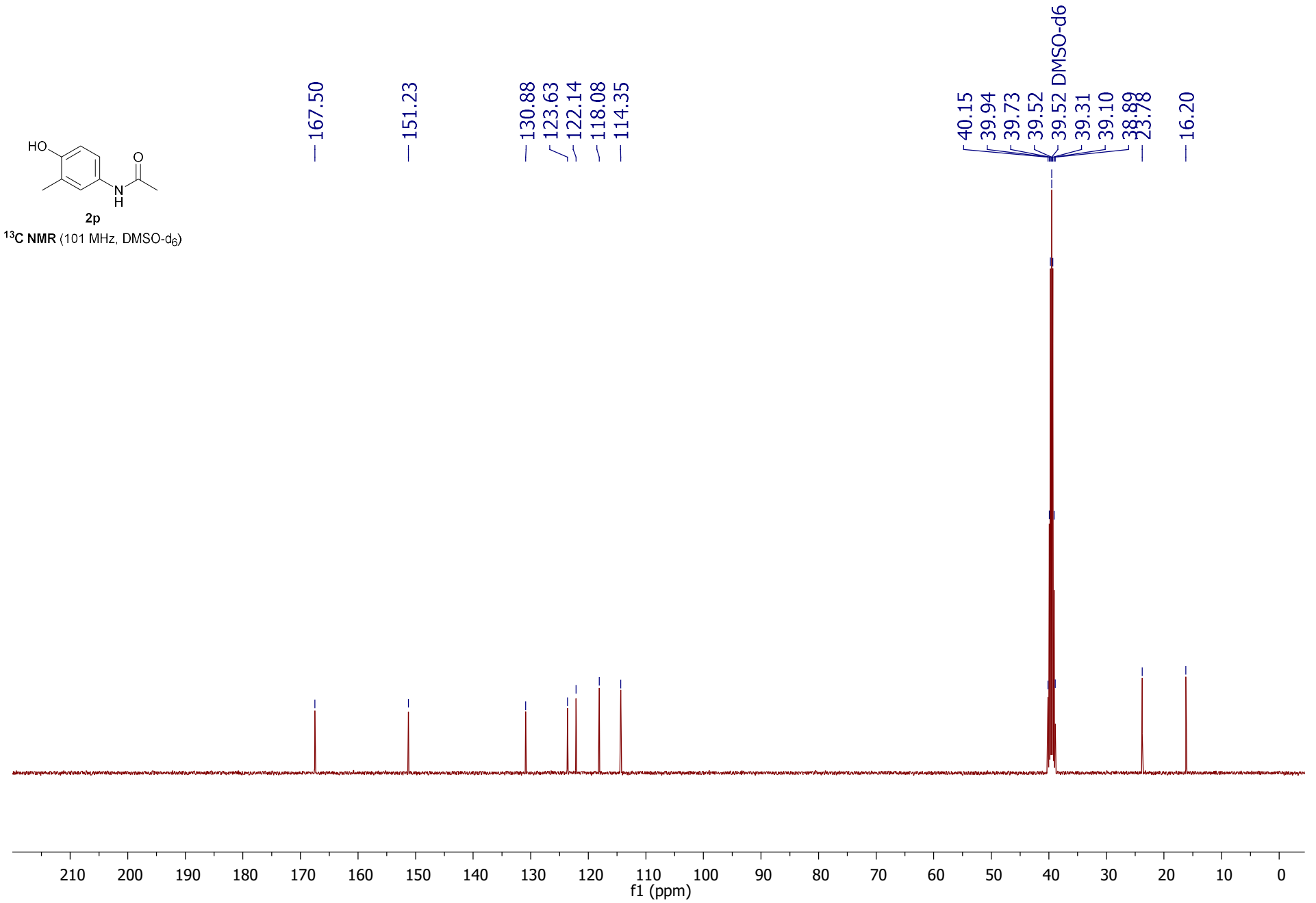
2n

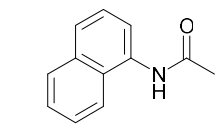
^{13}**C NMR** (101 MHz, DMSO-d_6)


HO
O
N
H
2o
1H NMR (400 MHz, DMSO-d6)
9.64
9.13
7.34
7.32
6.68
6.67
6.66
3.37
2.50 DMSO-d6
1.97
1.00
1.00
2.01
2.09
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


HO
O
N
H
2o
13C NMR (101 MHz, DMSO-d6)
167.57
153.14
131.06
120.84
115.02
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
23.77
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

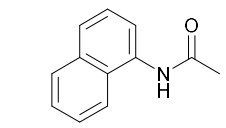

HO
O
N
H
2p
1H NMR (400 MHz, DMSO-d6)
9.57
9.02
7.23
7.23
7.17
7.16
7.14
7.14
6.67
6.65
3.38
2.50 DMSO-d6
2.07
1.96
1.00
1.00
1.00
1.00
1.00
3.00
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


HO
O
N
H
2p
13C NMR (101 MHz, DMSO-d6)
167.50
151.23
130.88
123.63
122.14
118.08
114.35
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
23.78
16.20
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



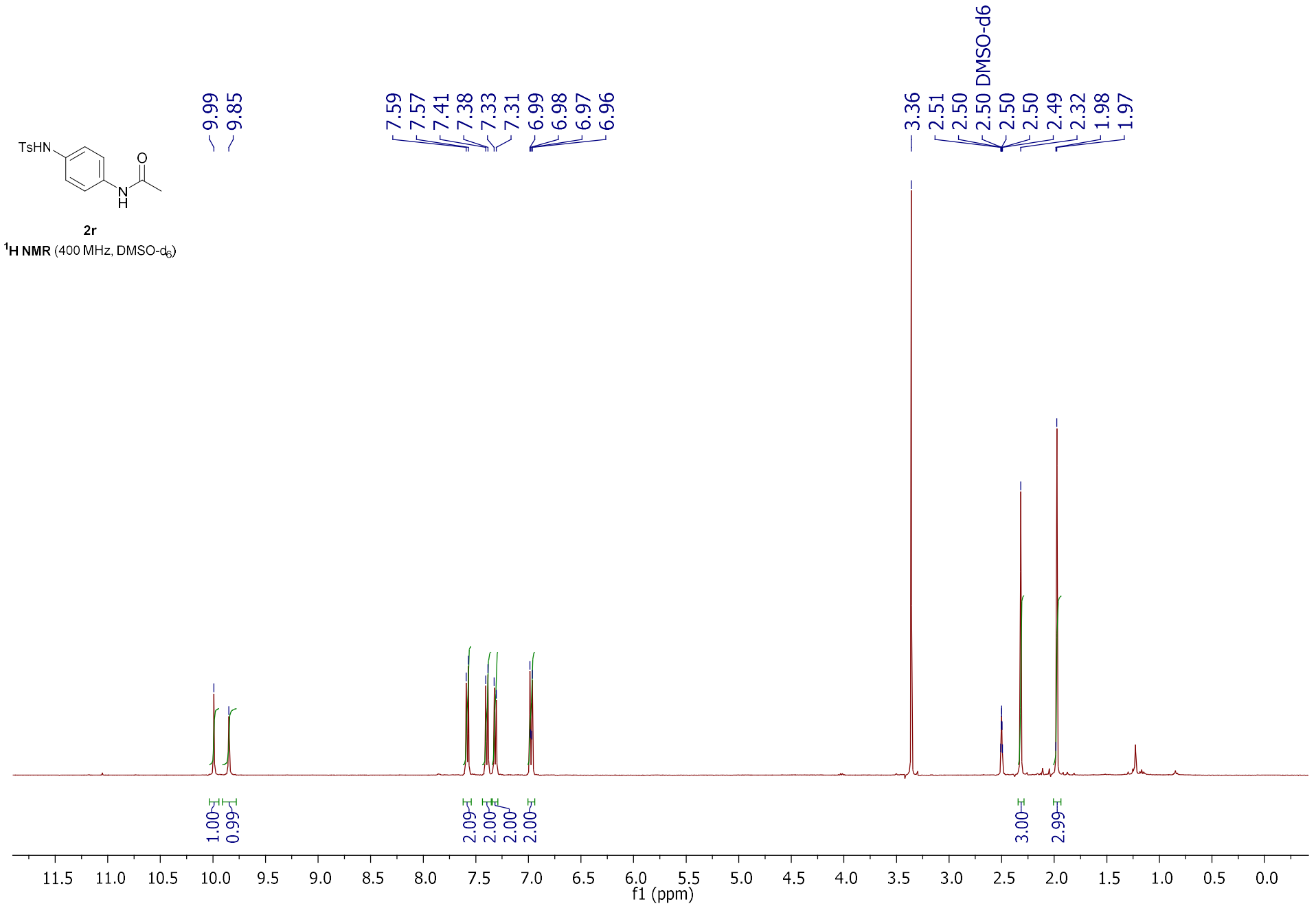
2q

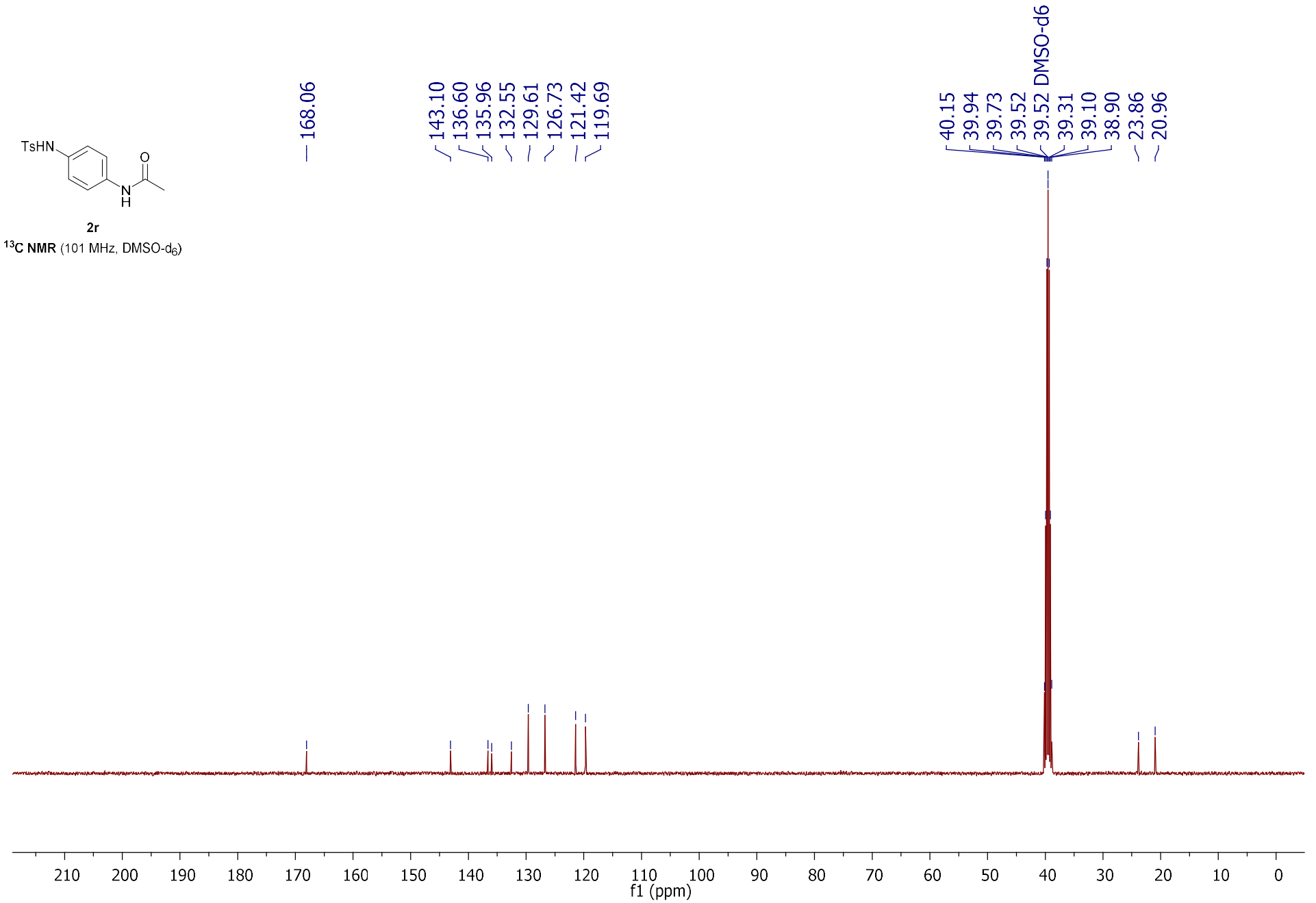
^{1}H NMR (400 MHz, DMSO-d_6)

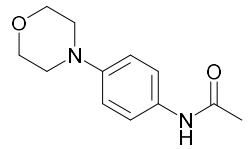


2q

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

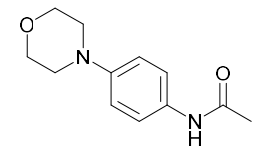

TsHN
O
N
H
2r
1H NMR (400 MHz, DMSO-d6)
9.99
9.85
7.59
7.57
7.41
7.38
7.33
7.31
6.99
6.98
6.97
6.96
3.36
2.51
2.50
2.50 DMSO-d6
2.50
2.50
2.49
2.32
1.98
1.97
1.00
0.99
2.09
2.00
2.00
2.00
3.00
2.99
f1 (ppm)


TsHN
O
N
H
2r
13C NMR (101 MHz, DMSO-d6)
168.06
143.10
136.60
135.96
132.55
129.61
126.73
121.42
119.69
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.90
23.86
20.96
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



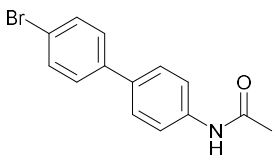
2s

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



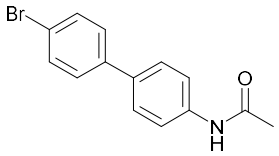
2s

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



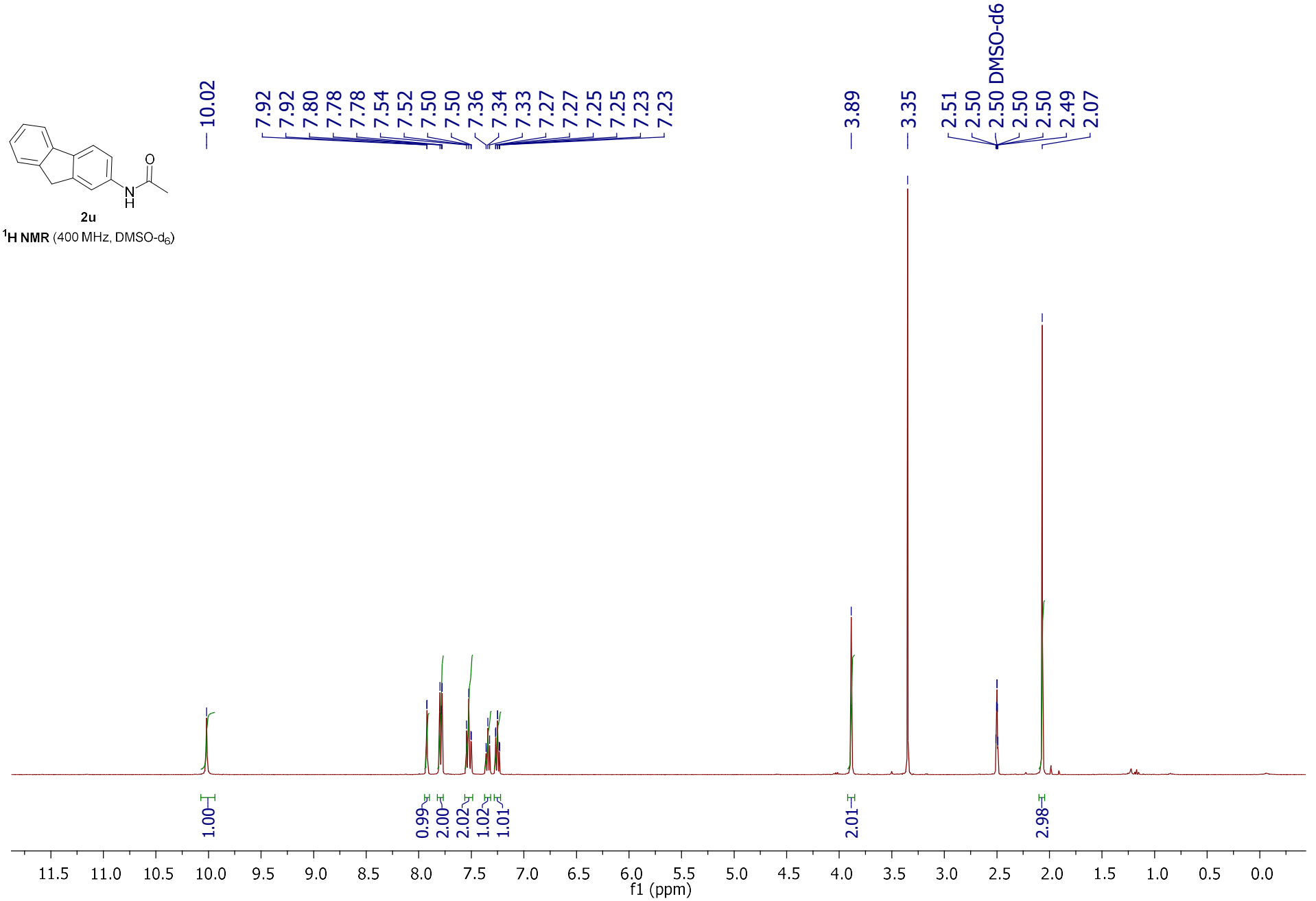
2t

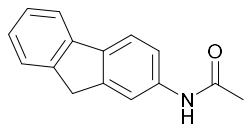
^{1}H NMR (400 MHz, DMSO-d_6)



2t

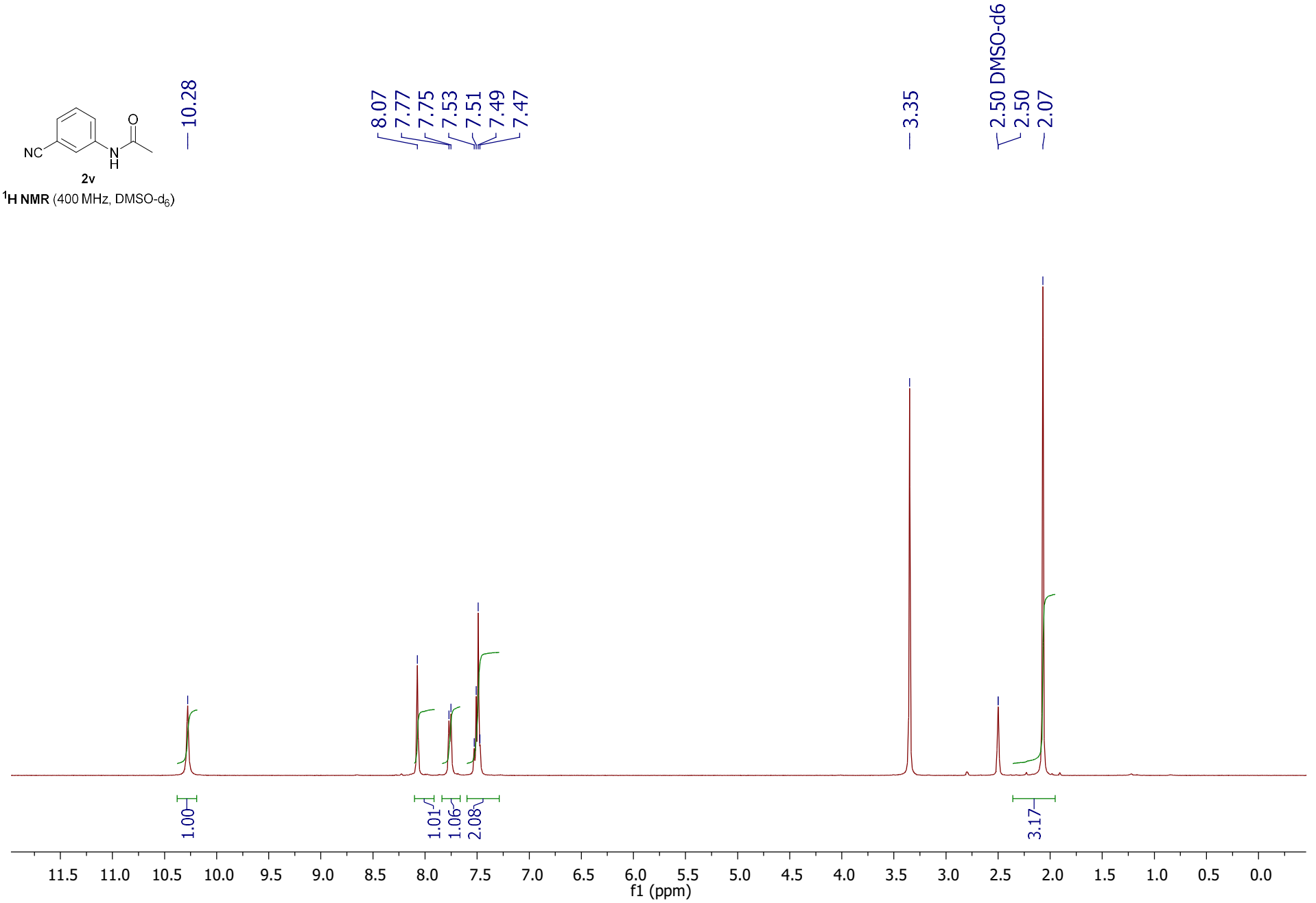
^{13}C NMR (101 MHz, DMSO-d_6)

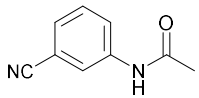

10.02
7.92
7.92
7.80
7.78
7.78
7.54
7.52
7.50
7.50
7.36
7.34
7.33
7.27
7.27
7.25
7.25
7.23
7.23
3.89
3.35
2.51
2.50
2.50 DMSO-d6
2.50
2.50
2.49
2.07
O
N
H
2u
1H NMR (400 MHz, DMSO-d6)
1.00
0.99
2.00
2.02
1.02
1.01
2.01
2.98
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



2u

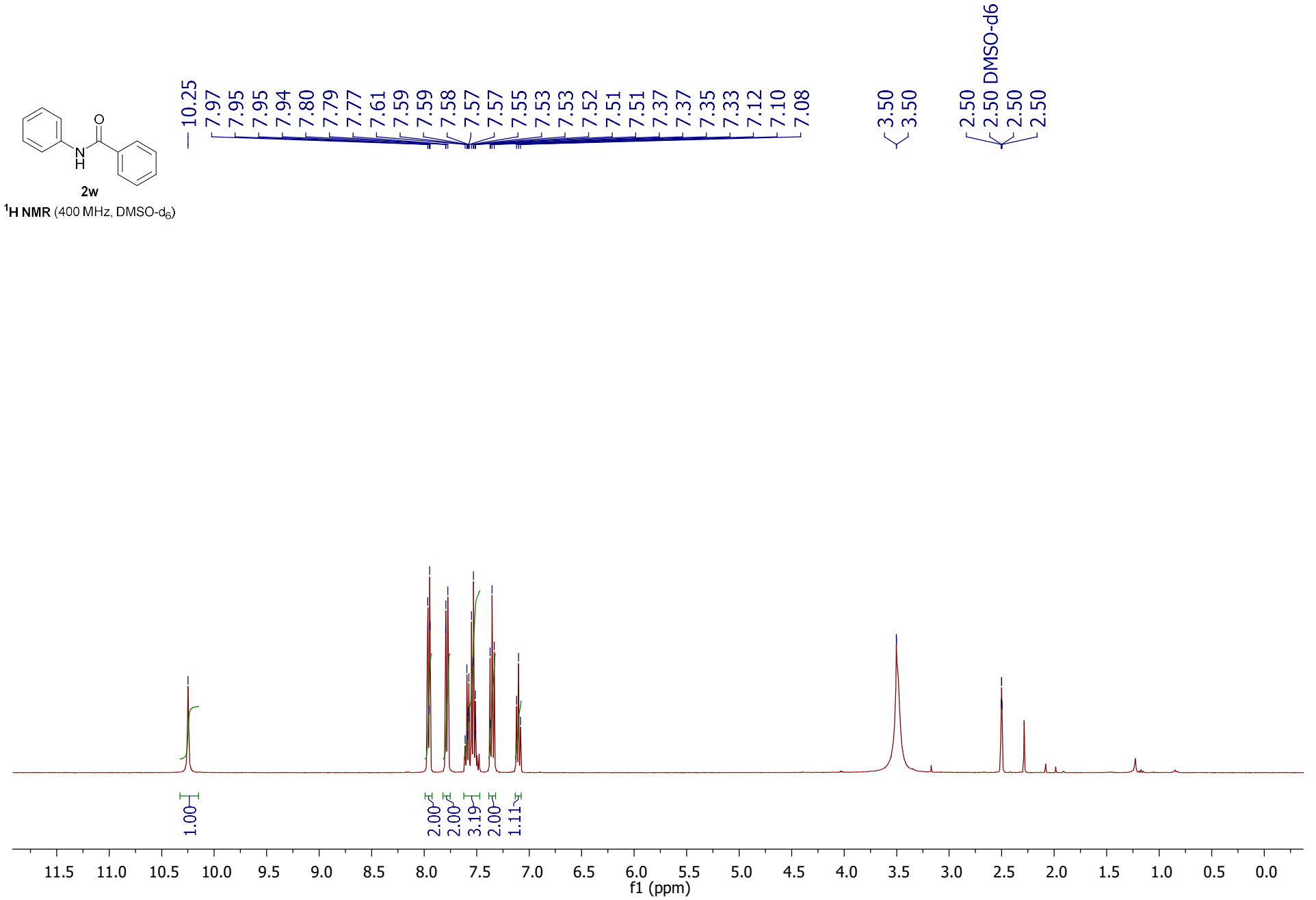
^{13}C NMR (101 MHz, DMSO-d_6)

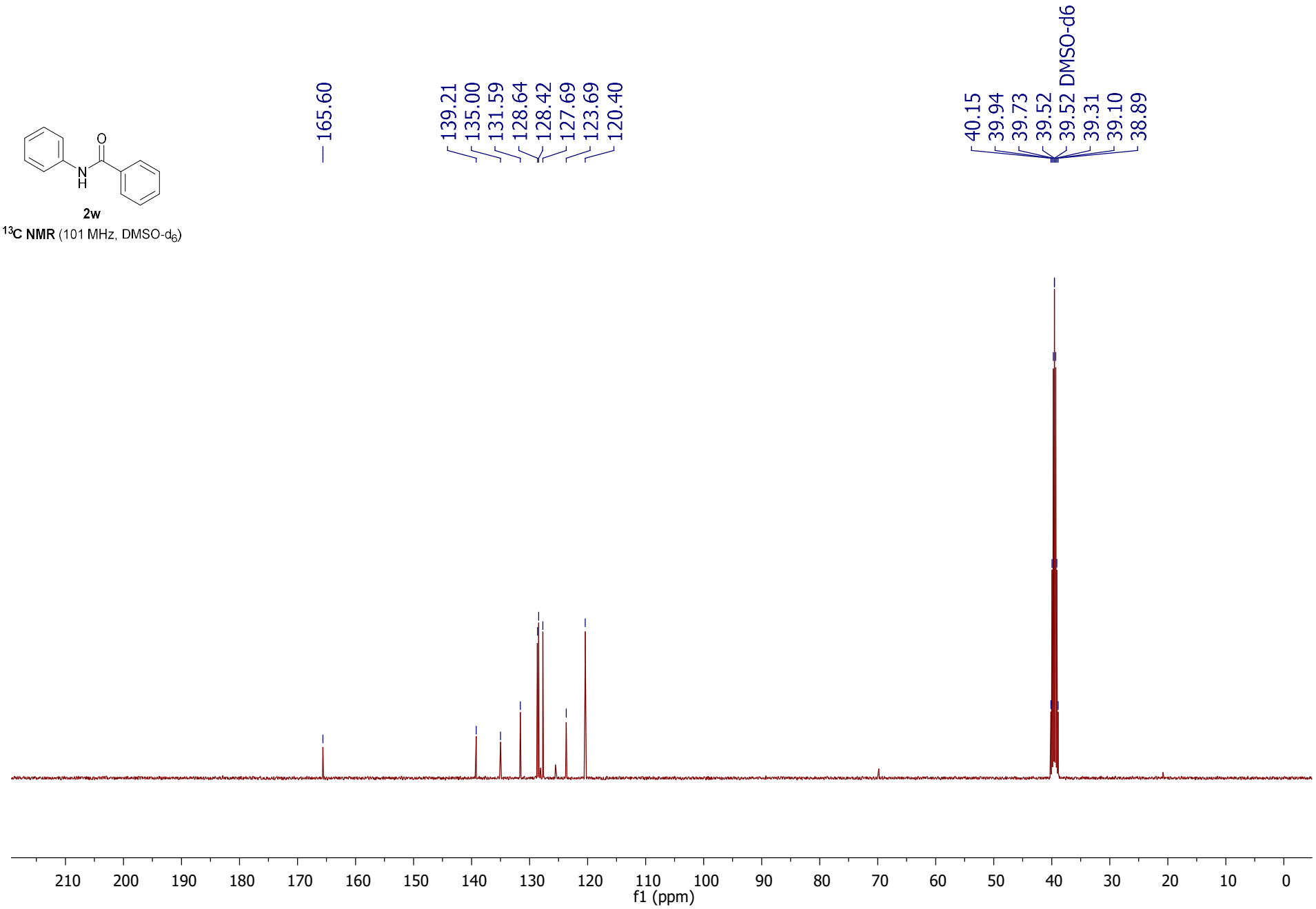

NC
N
H
O
2v
1H NMR (400 MHz, DMSO-d6)
10.28
8.07
7.77
7.75
7.53
7.51
7.49
7.47
3.35
2.50 DMSO-d6
2.50
2.07
1.00
1.01
1.06
2.08
3.17
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

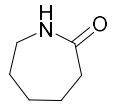


2v

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

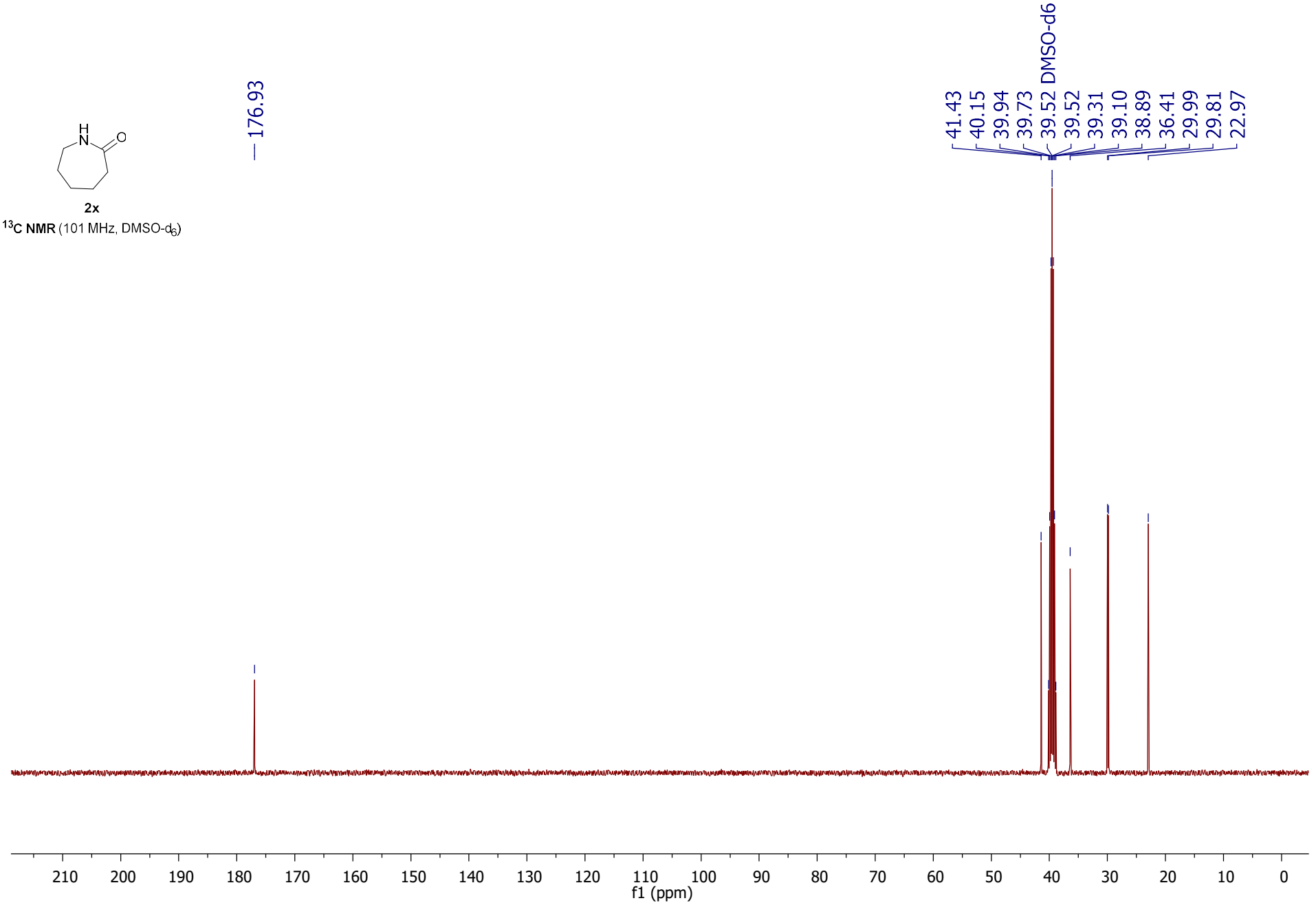

2w
1H NMR (400 MHz, DMSO-d6)
10.25
7.97
7.95
7.95
7.94
7.80
7.79
7.77
7.61
7.59
7.59
7.58
7.57
7.57
7.55
7.53
7.53
7.52
7.51
7.51
7.37
7.37
7.35
7.33
7.12
7.10
7.08
3.50
3.50
2.50
2.50 DMSO-d6
2.50
2.50
1.00
2.00
2.00
3.19
2.00
1.11
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

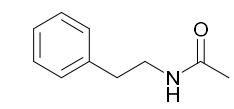

165.60
139.21
135.00
131.59
128.64
128.42
127.69
123.69
120.40
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
O
N
H
2w
13C NMR (101 MHz, DMSO-d6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



2x

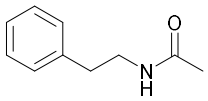
^{1}H NMR (400 MHz, DMSO-d_6)


H
N
O
2x
13C NMR (101 MHz, DMSO-d6)
176.93
41.43
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
36.41
29.99
29.81
22.97
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



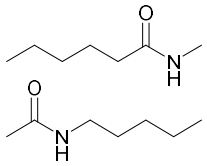
2y

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



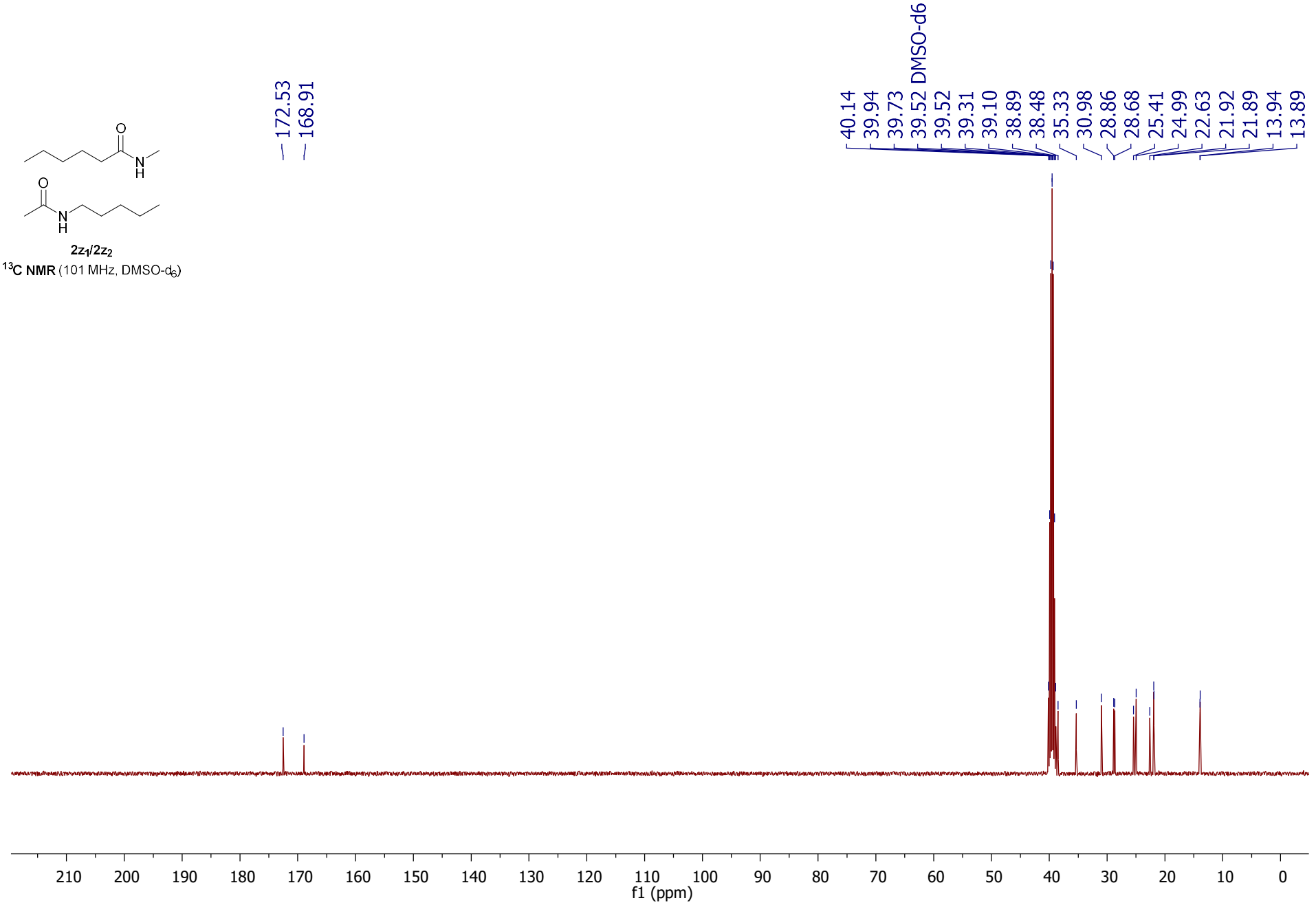
2y

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



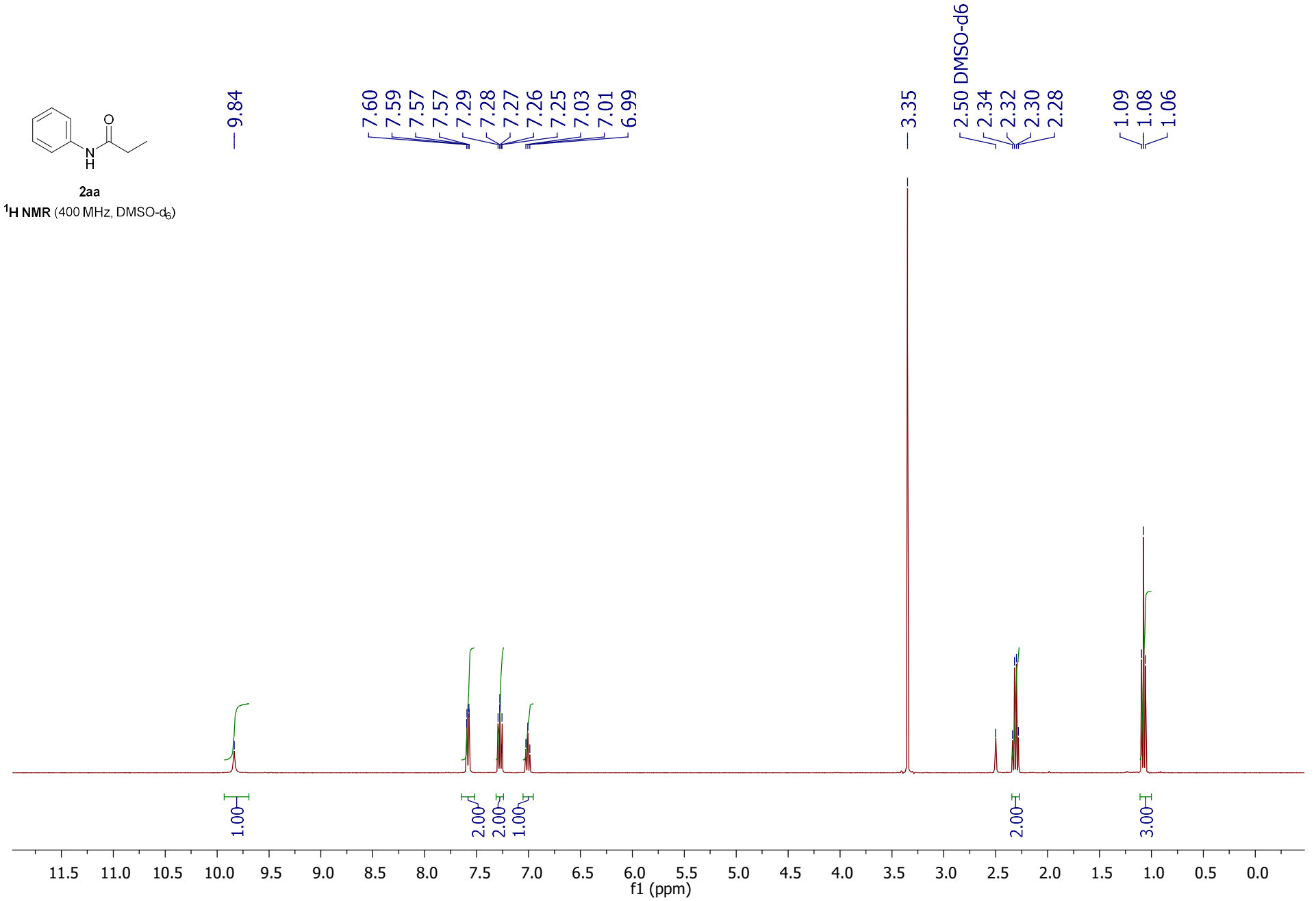
$2z_1/2z_2$

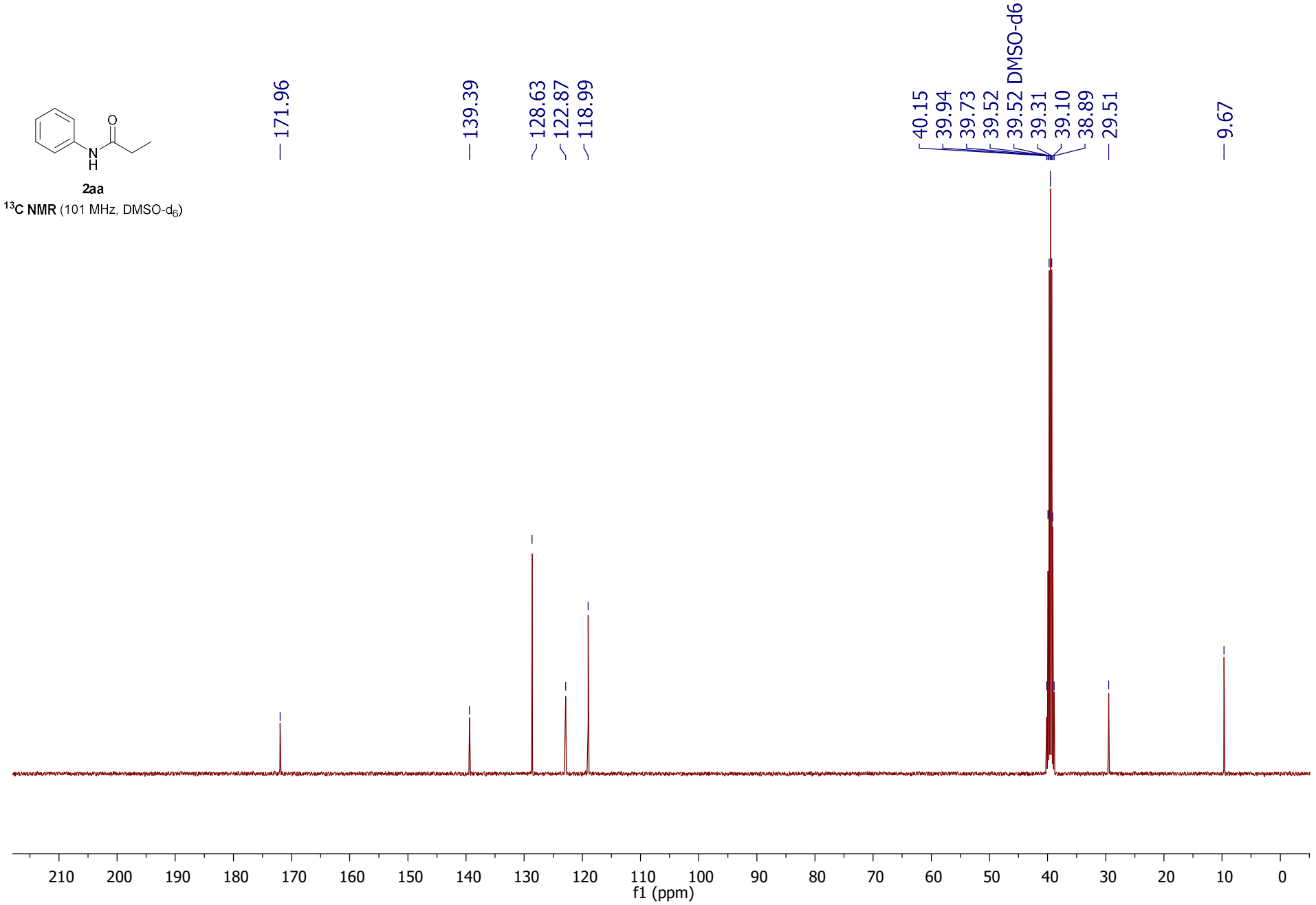
^{1}H NMR (400 MHz, DMSO-d_6)

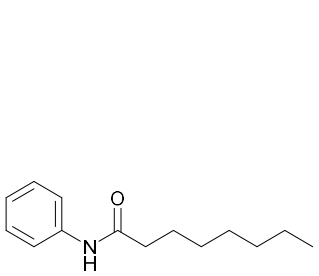


2z$_1$/2z$_2$

^{13}C NMR (101 MHz, DMSO-d$_6$)

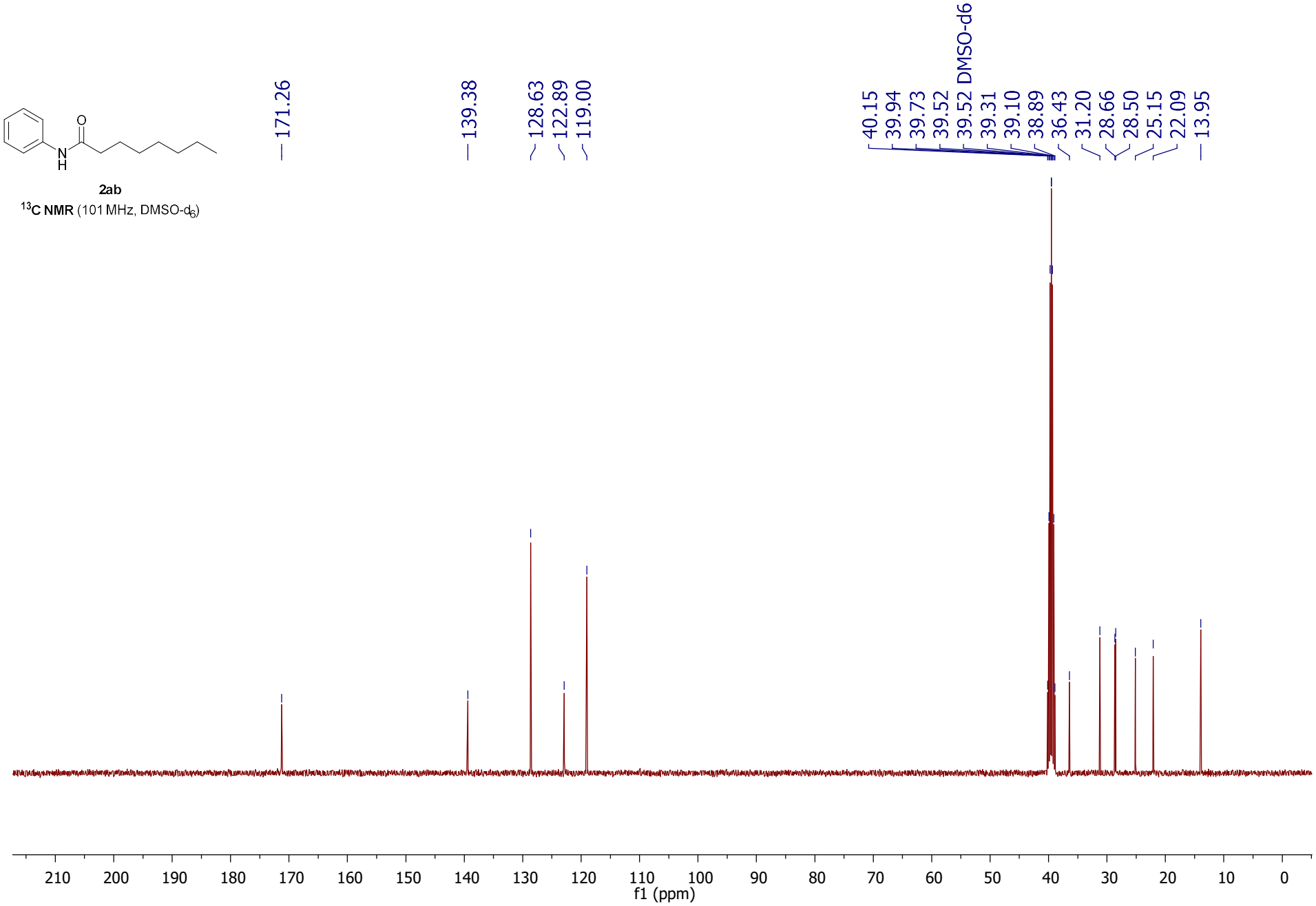

2aa
1H NMR (400 MHz, DMSO-d6)
9.84
7.60
7.59
7.57
7.57
7.29
7.28
7.27
7.26
7.25
7.03
7.01
6.99
3.35
2.50 DMSO-d6
2.34
2.32
2.30
2.28
1.09
1.08
1.06
1.00
2.00
2.00
1.00
2.00
3.00
f1 (ppm)

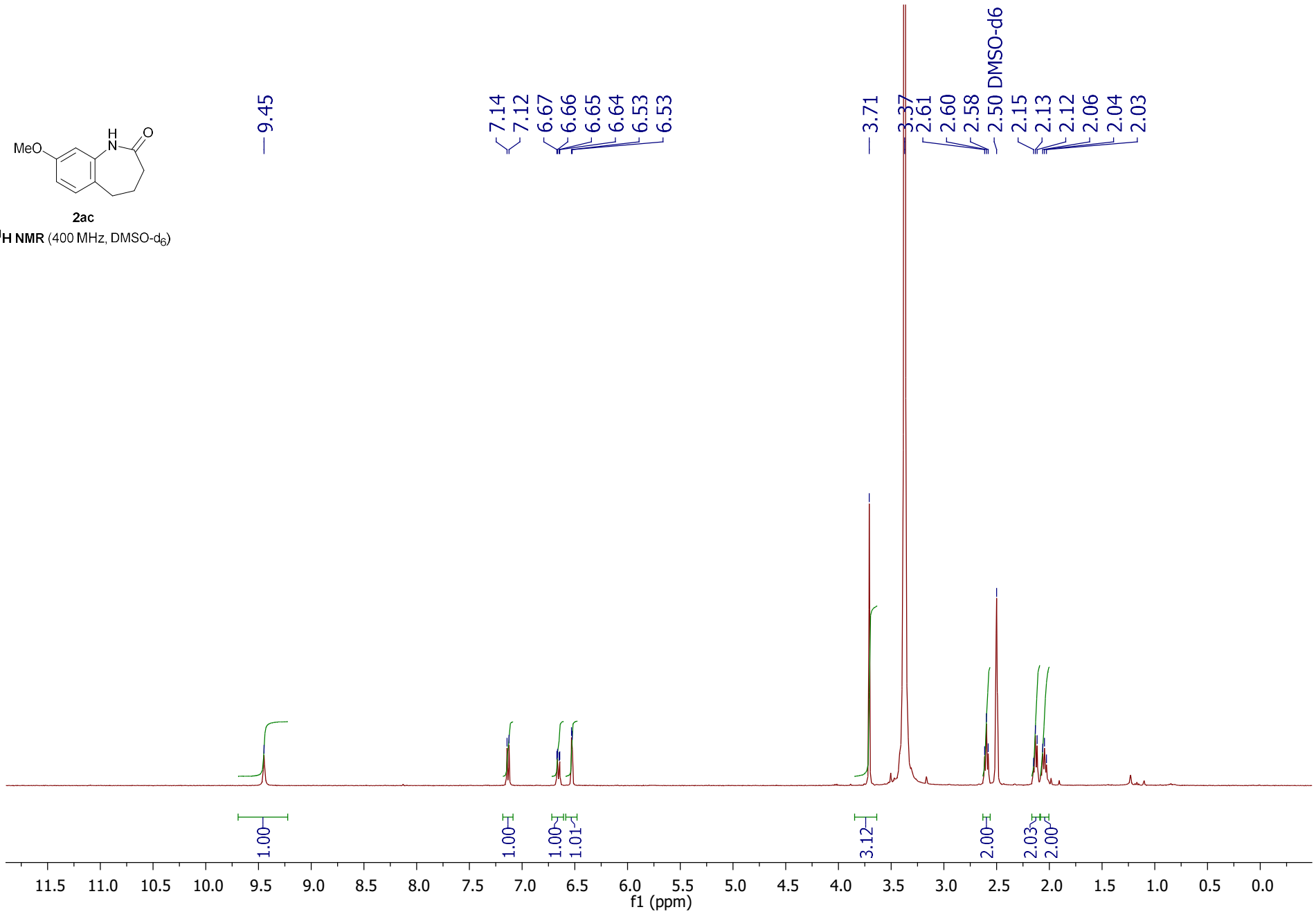

171.96
139.39
128.63
122.87
118.99
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
29.51
9.67
2aa
13C NMR (101 MHz, DMSO-d6)
f1 (ppm)

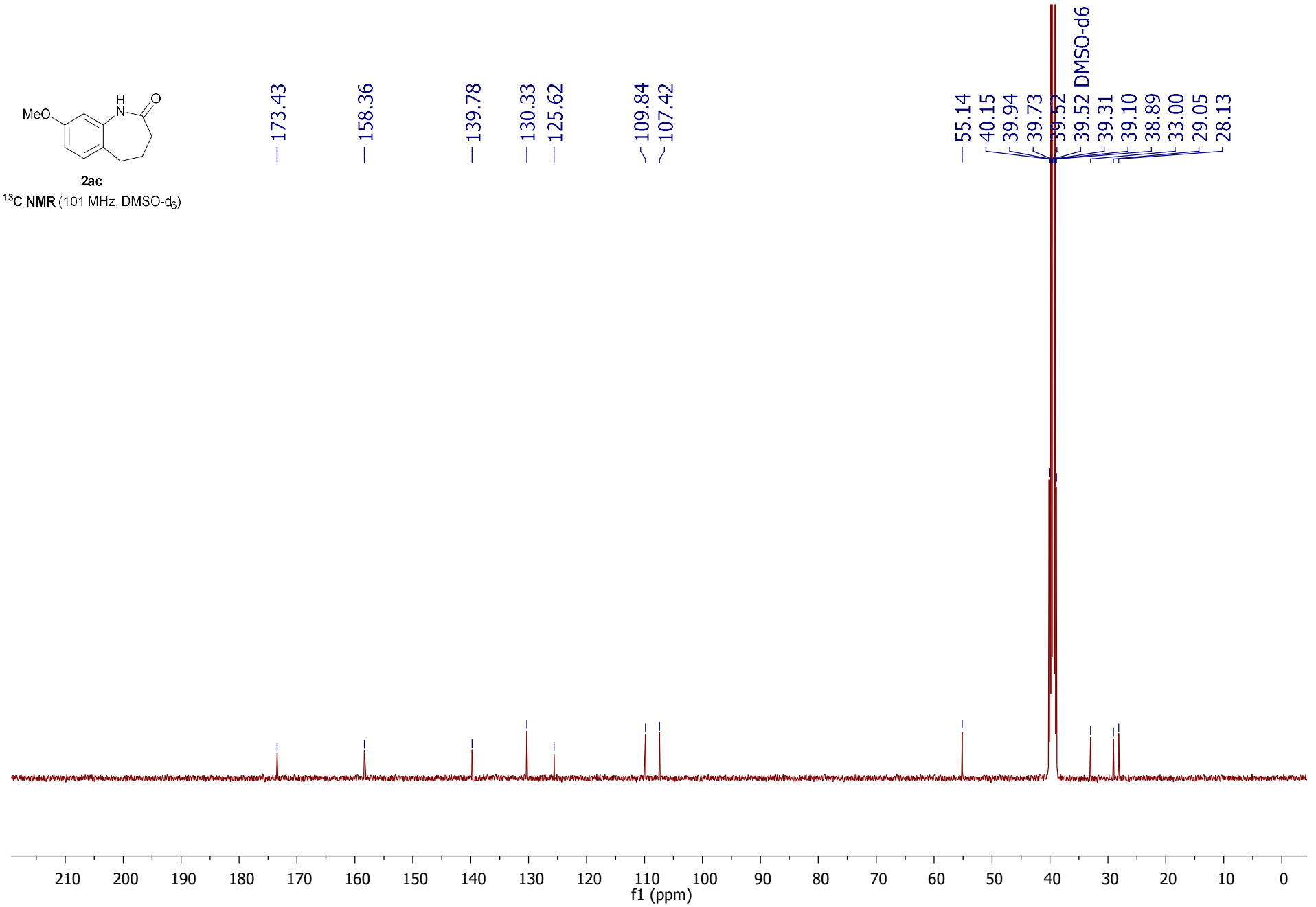


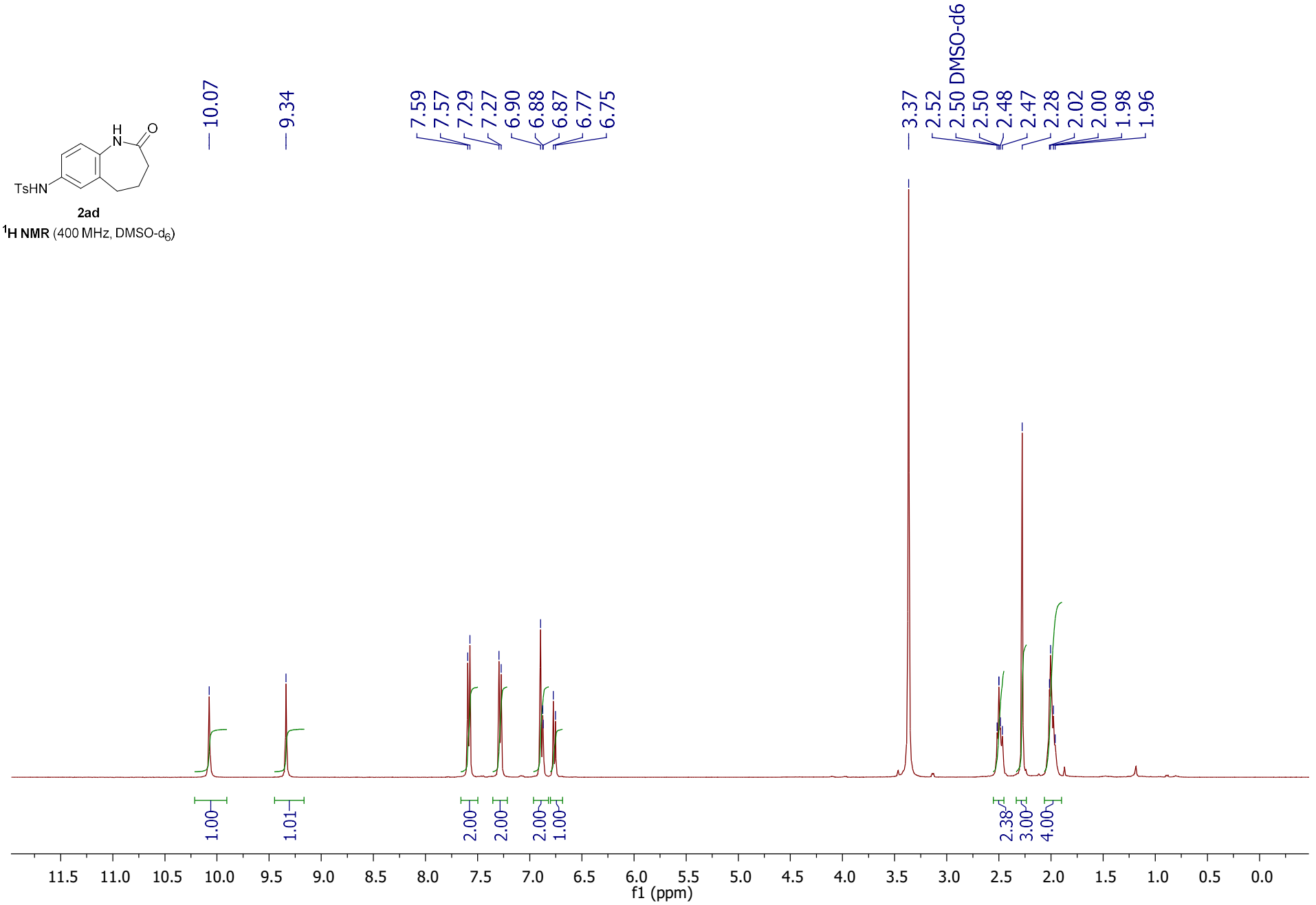
2ab

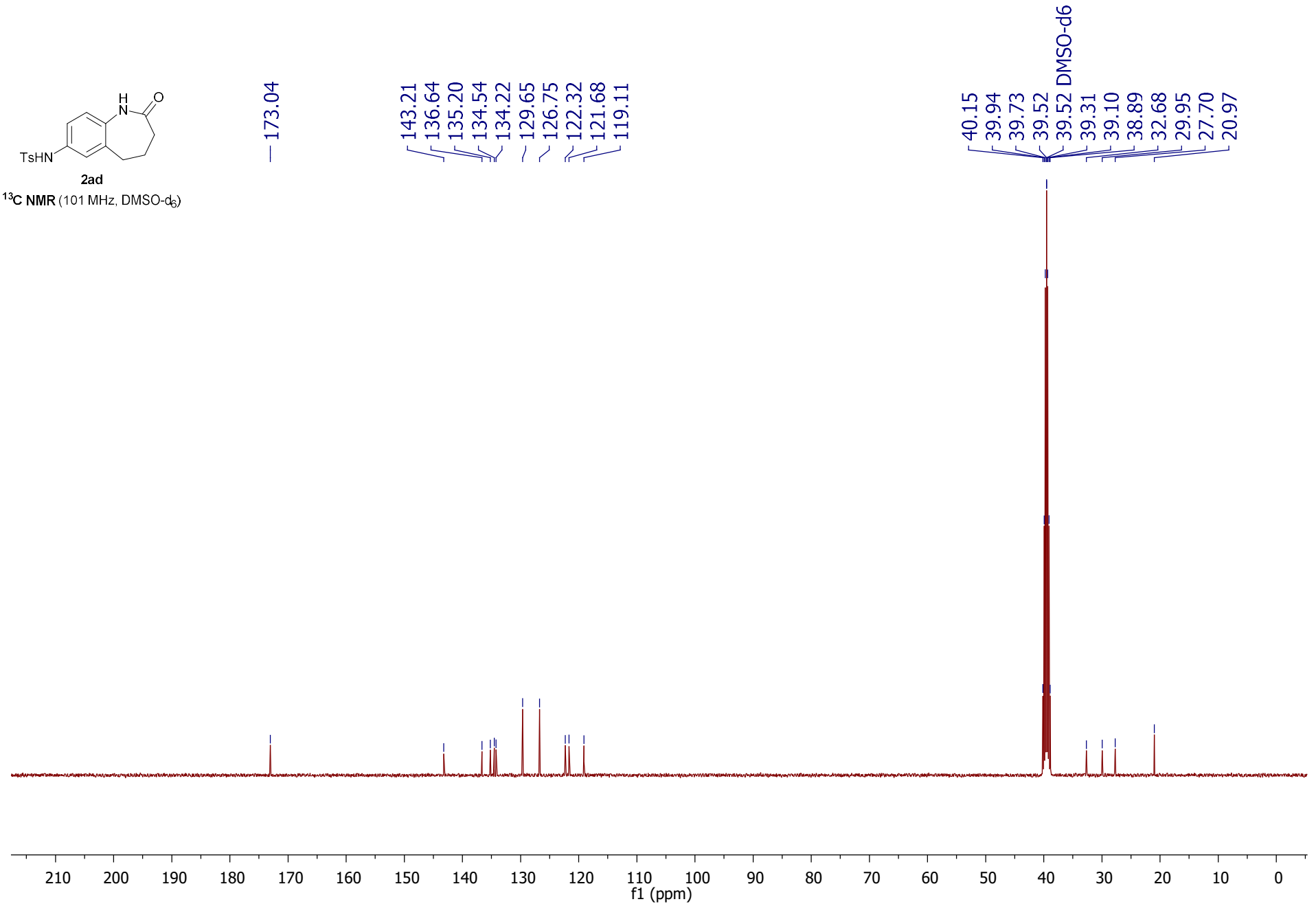
^{1}H NMR (400 MHz, DMSO-d_6)

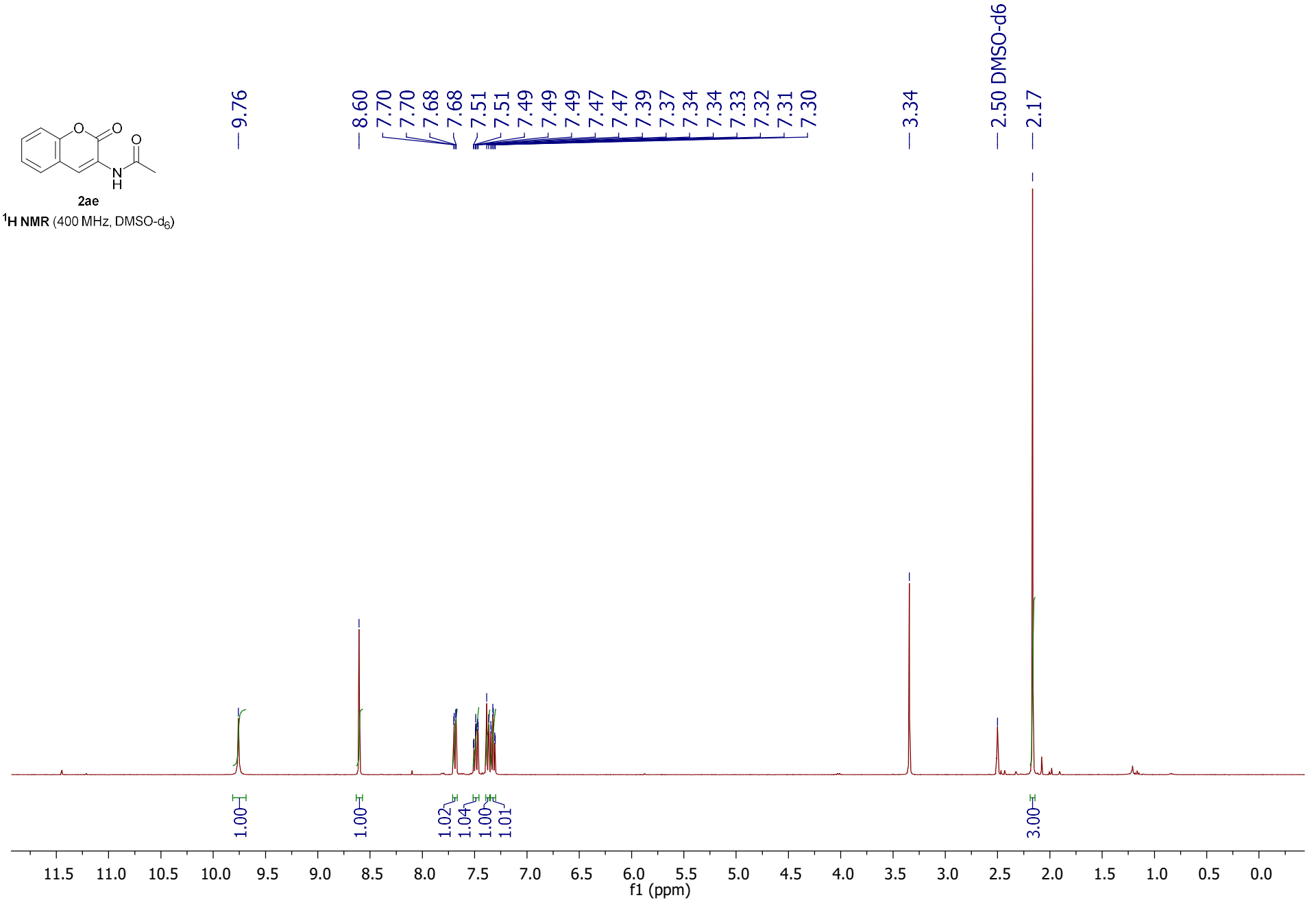

171.26
139.38
128.63
122.89
119.00
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
36.43
31.20
28.66
28.50
25.15
22.09
13.95
O
N
H
2ab
13C NMR (101 MHz, DMSO-d6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

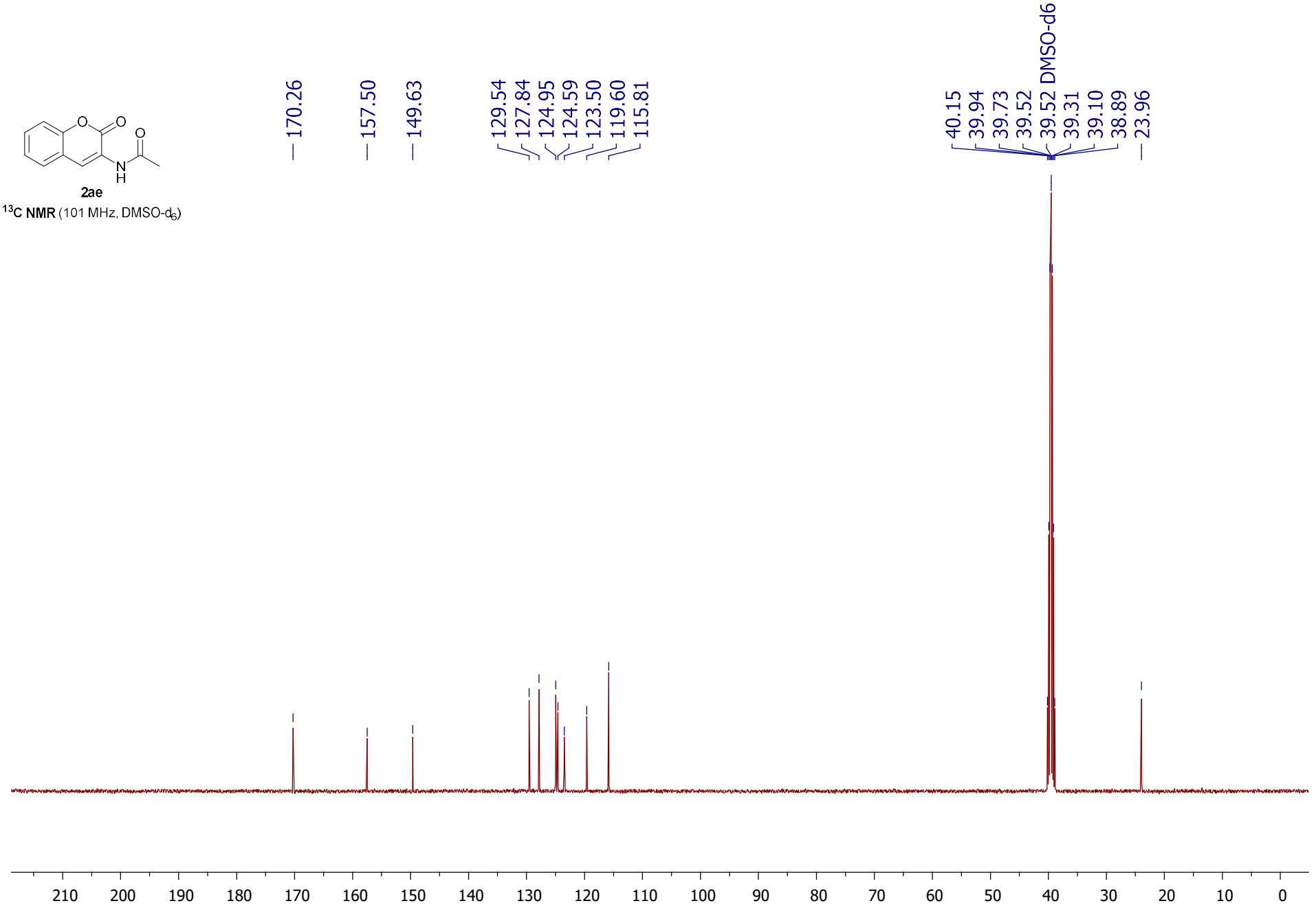

MeO
H
N
O
2ac
1H NMR (400 MHz, DMSO-d6)
9.45
7.14
7.12
6.67
6.66
6.65
6.64
6.53
6.53
3.71
3.37
2.61
2.60
2.58
2.50 DMSO-d6
2.15
2.13
2.12
2.06
2.04
2.03
1.00
1.00
1.00
1.01
3.12
2.00
2.03
2.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

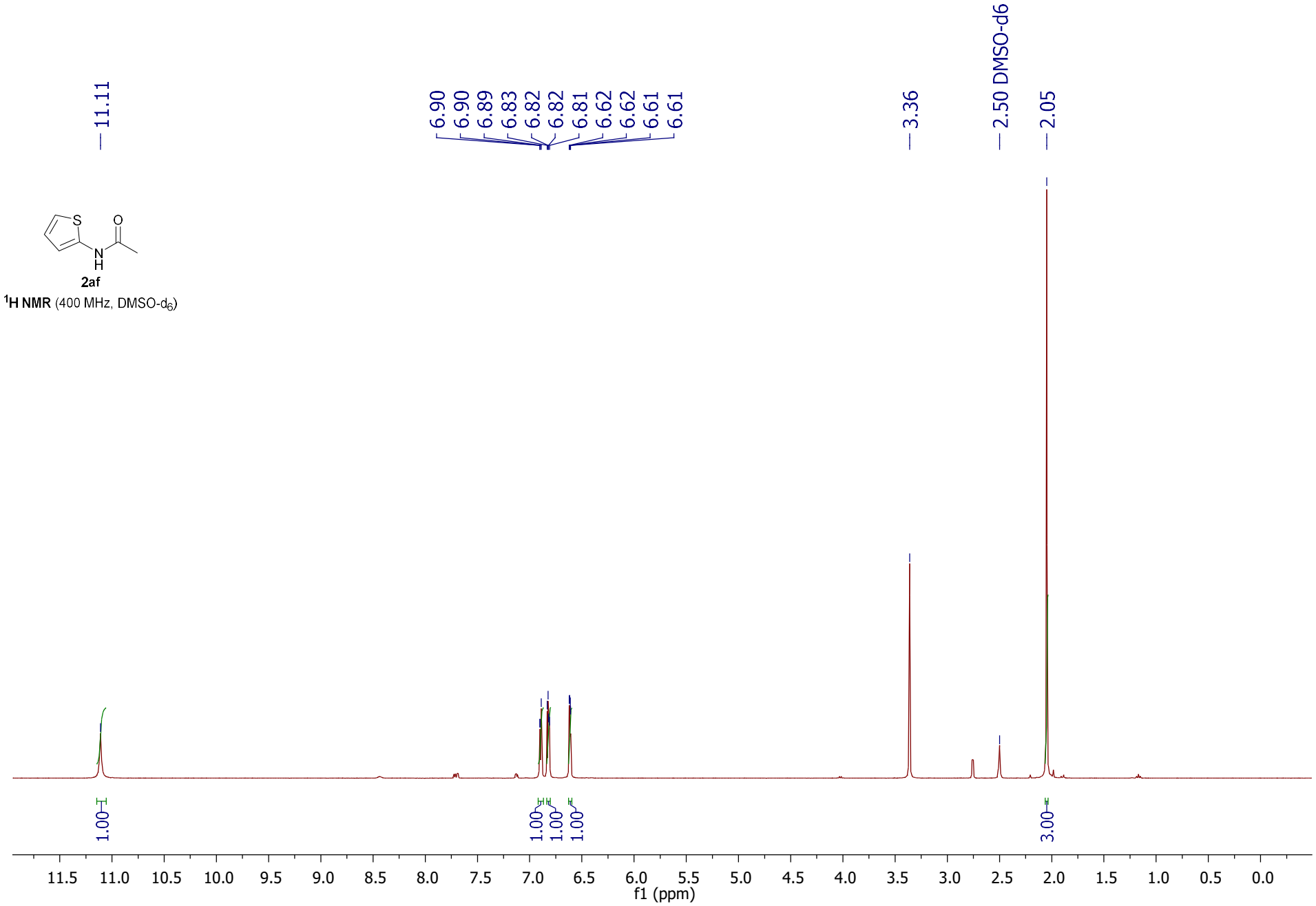

MeO
H
N
O
2ac
13C NMR (101 MHz, DMSO-d6)
173.43
158.36
139.78
130.33
125.62
109.84
107.42
55.14
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
33.00
29.05
28.13
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

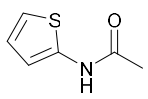

TsHN
H
N
O
2ad
1H NMR (400 MHz, DMSO-d6)
10.07
9.34
7.59
7.57
7.29
7.27
6.90
6.88
6.87
6.77
6.75
3.37
2.52
2.50 DMSO-d6
2.50
2.48
2.47
2.28
2.02
2.00
1.98
1.96
1.00
1.01
2.00
2.00
2.00
1.00
2.38
3.00
4.00
f1 (ppm)


TsHN
2ad
13C NMR (101 MHz, DMSO-d6)
173.04
143.21
136.64
135.20
134.54
134.22
129.65
126.75
122.32
121.68
119.11
40.15
39.94
39.73
39.52
DMSO-d6
39.31
39.10
38.89
32.68
29.95
27.70
20.97
f1 (ppm)


2ae
1H NMR (400 MHz, DMSO-d6)
9.76
8.60
7.70
7.70
7.68
7.68
7.51
7.51
7.49
7.49
7.49
7.47
7.47
7.39
7.37
7.34
7.34
7.33
7.32
7.31
7.30
3.34
2.50 DMSO-d6
2.17
1.00
1.00
1.02
1.04
1.00
1.01
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

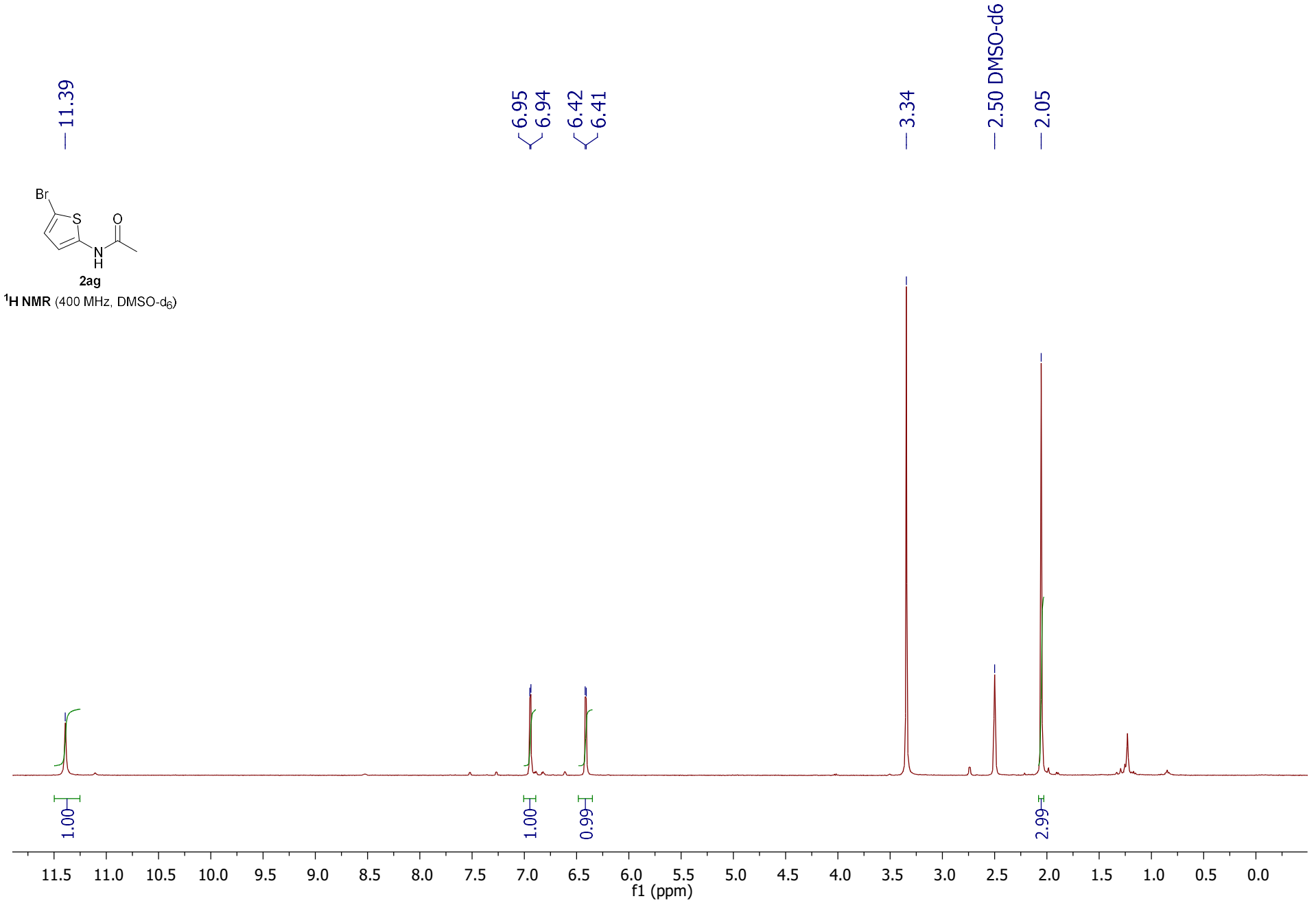

2ae
13C NMR (101 MHz, DMSO-d6)
170.26
157.50
149.63
129.54
127.84
124.95
124.59
123.50
119.60
115.81
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
23.96
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

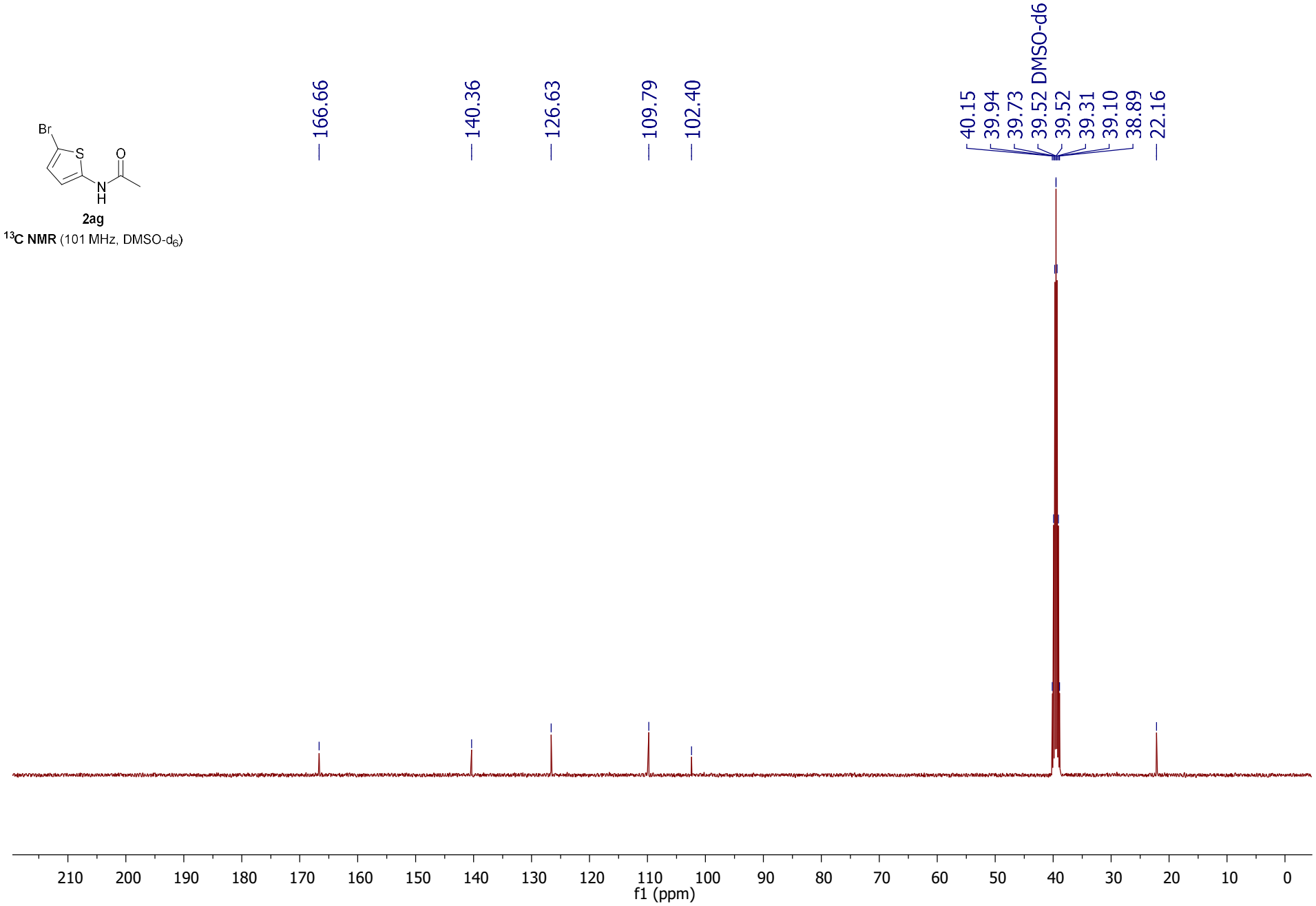

11.11
6.90
6.90
6.89
6.83
6.82
6.82
6.81
6.62
6.62
6.61
6.61
3.36
2.50 DMSO-d6
2.05
S
O
N
H
2af
1H NMR (400 MHz, DMSO-d6)
1.00
1.00
1.00
1.00
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

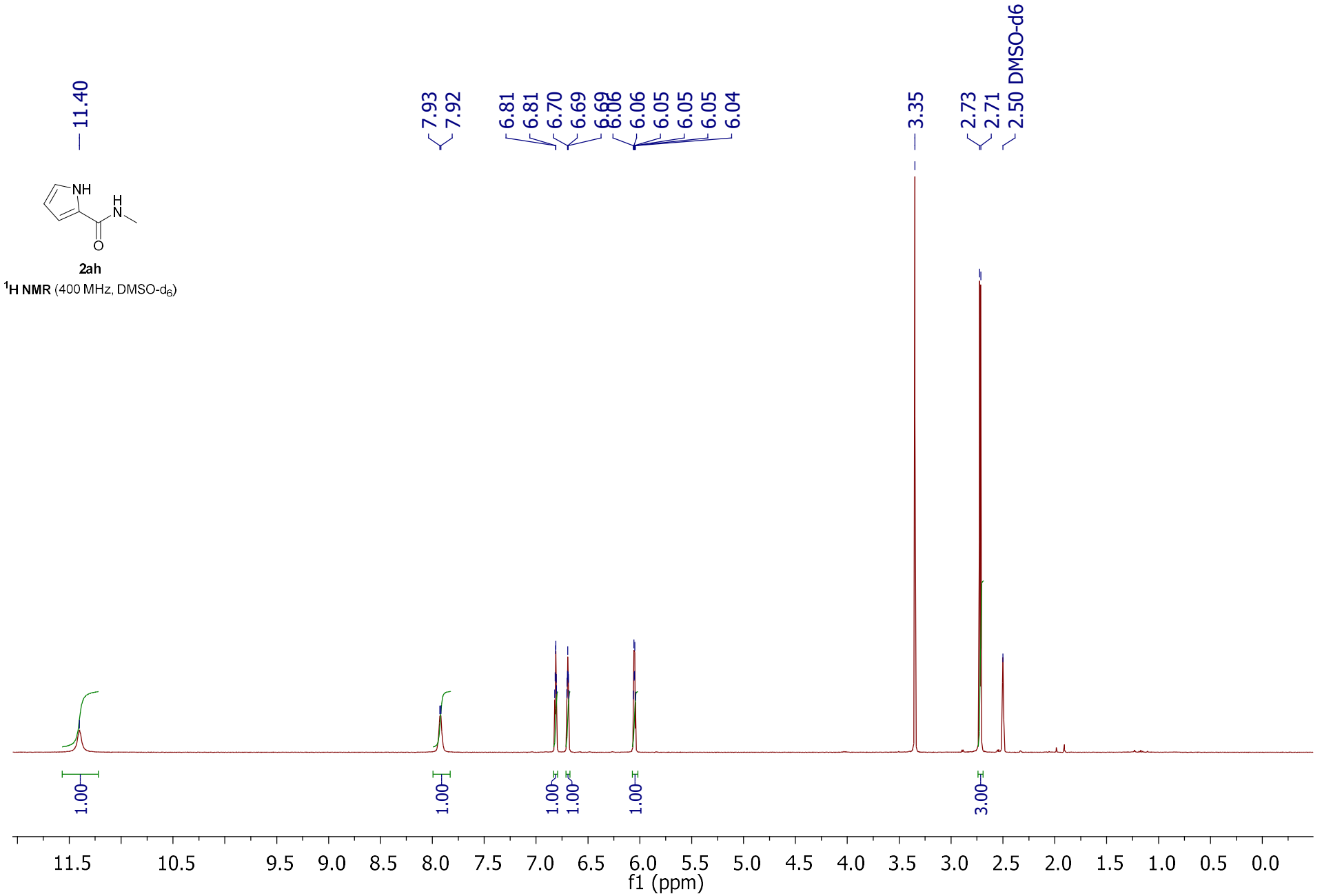


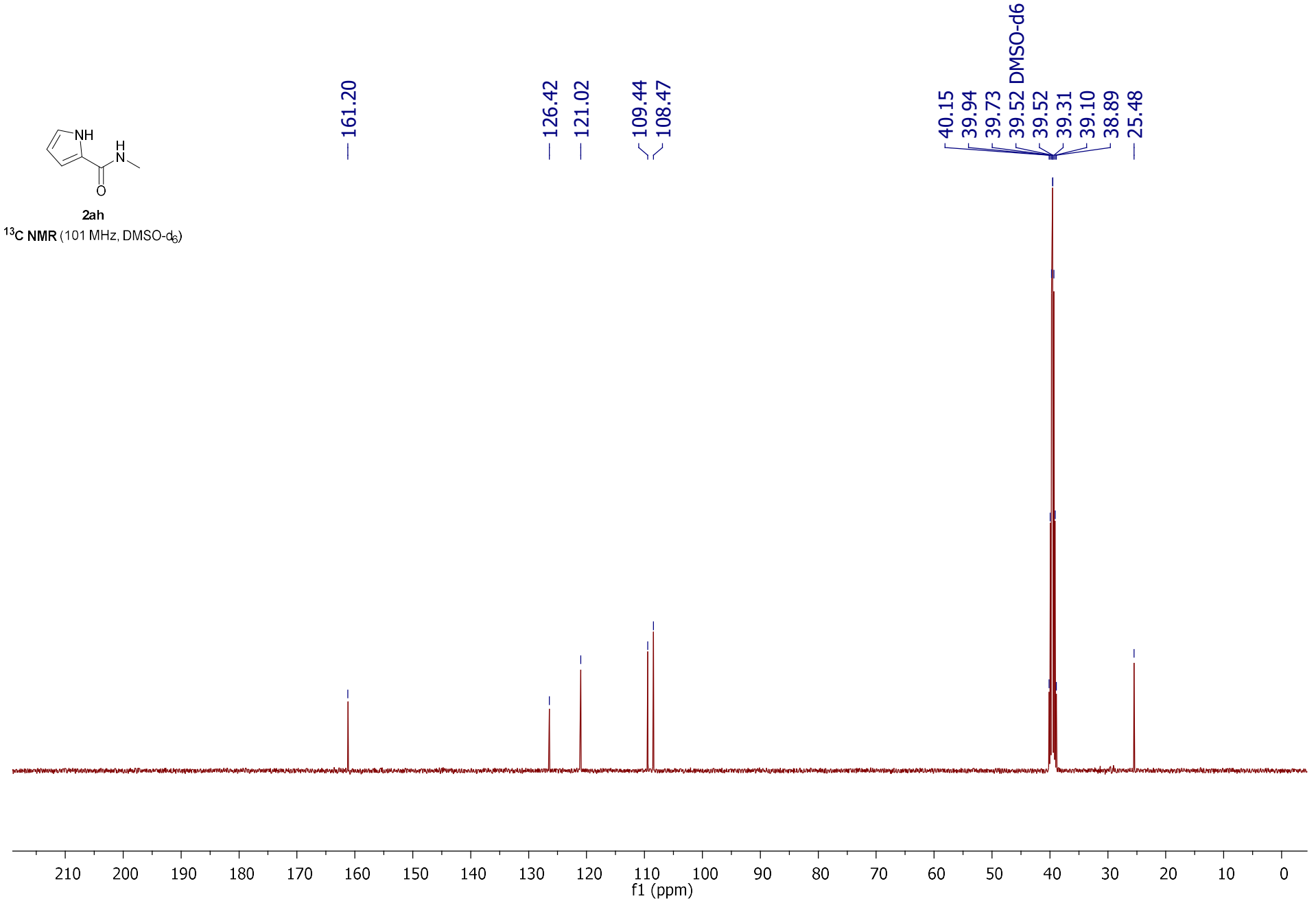
2af

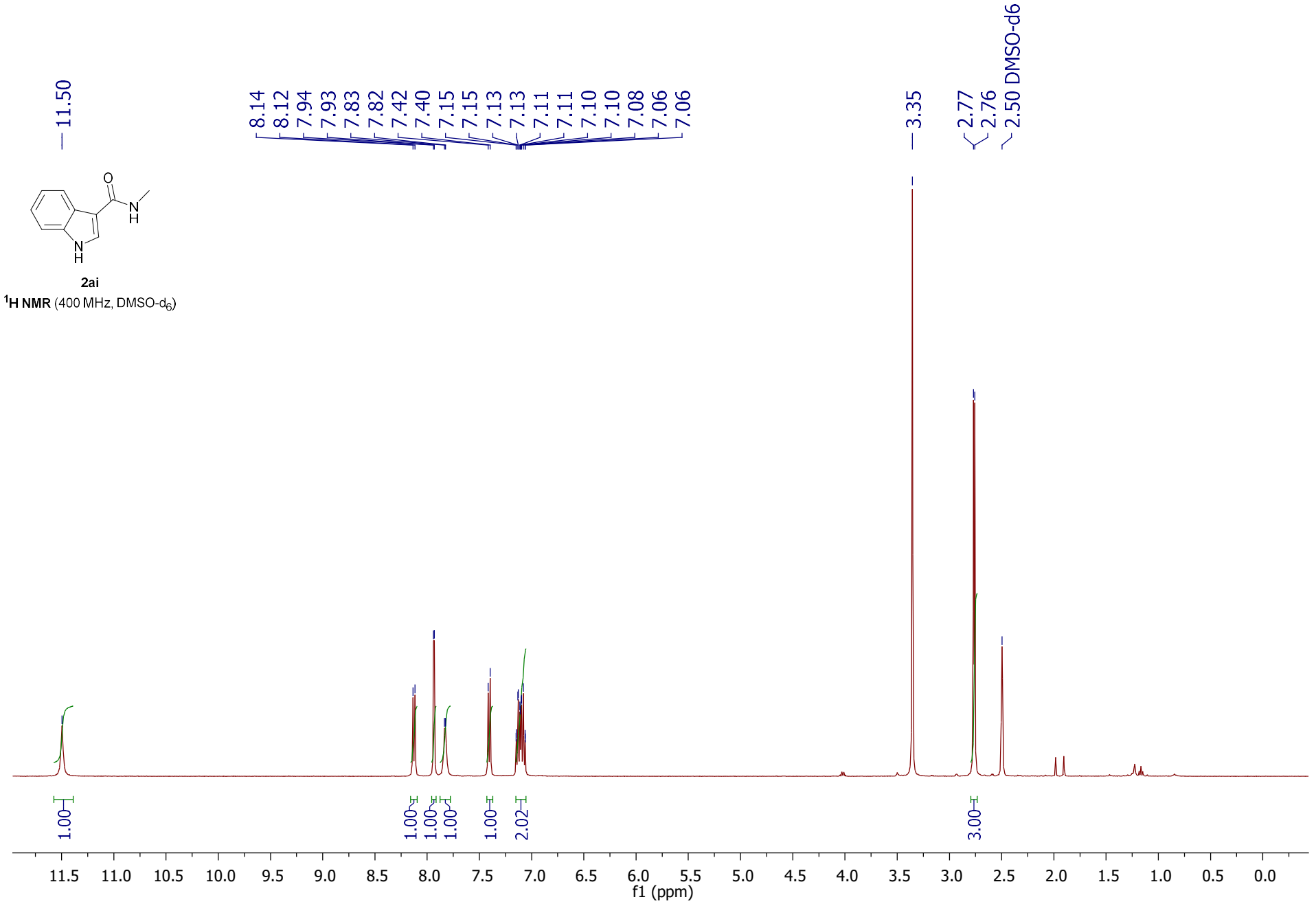
^{13}C NMR (101 MHz, DMSO-d_6)

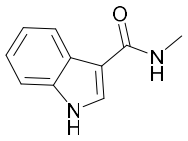

11.39
6.95
6.94
6.42
6.41
3.34
2.50 DMSO-d6
2.05
Br
S
O
N
H
2ag
1H NMR (400 MHz, DMSO-d6)
1.00
1.00
0.99
2.99
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Br
S
O
N
H
2ag
13C NMR (101 MHz, DMSO-d6)
166.66
140.36
126.63
109.79
102.40
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
22.16
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


11.40
7.93
7.92
6.81
6.81
6.70
6.69
6.06
6.05
6.05
6.05
6.04
3.35
2.73
2.71
2.50 DMSO-d6
NH
H
N
O
2ah
1H NMR (400 MHz, DMSO-d6)
1.00
1.00
1.00
1.00
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

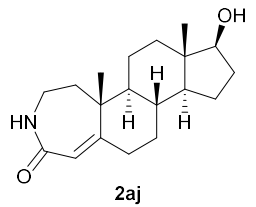

NH
H
N
O
2ah
13C NMR (101 MHz, DMSO-d6)
161.20
126.42
121.02
109.44
108.47
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
25.48
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


11.50
8.14
8.12
7.94
7.93
7.83
7.82
7.42
7.40
7.15
7.15
7.13
7.13
7.11
7.11
7.10
7.10
7.08
7.06
7.06
3.35
2.77
2.76
2.50 DMSO-d6
O
N
H
N
H
2ai
1H NMR (400 MHz, DMSO-d6)
1.00
1.00
1.00
1.00
2.02
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



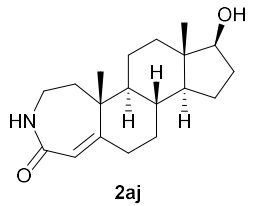
2ai

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



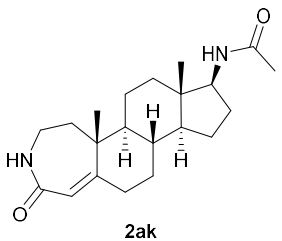
2aj

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



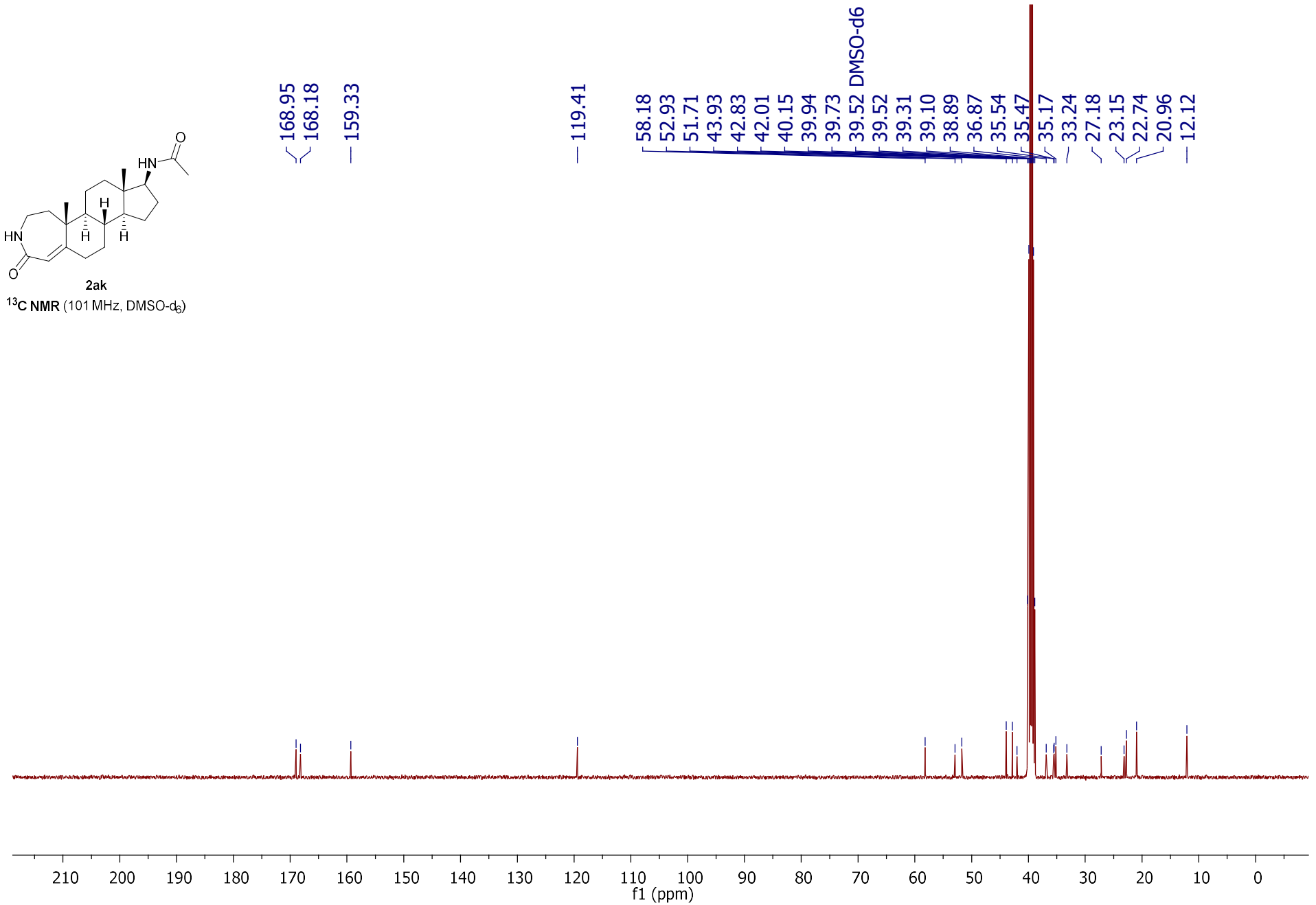
2aj

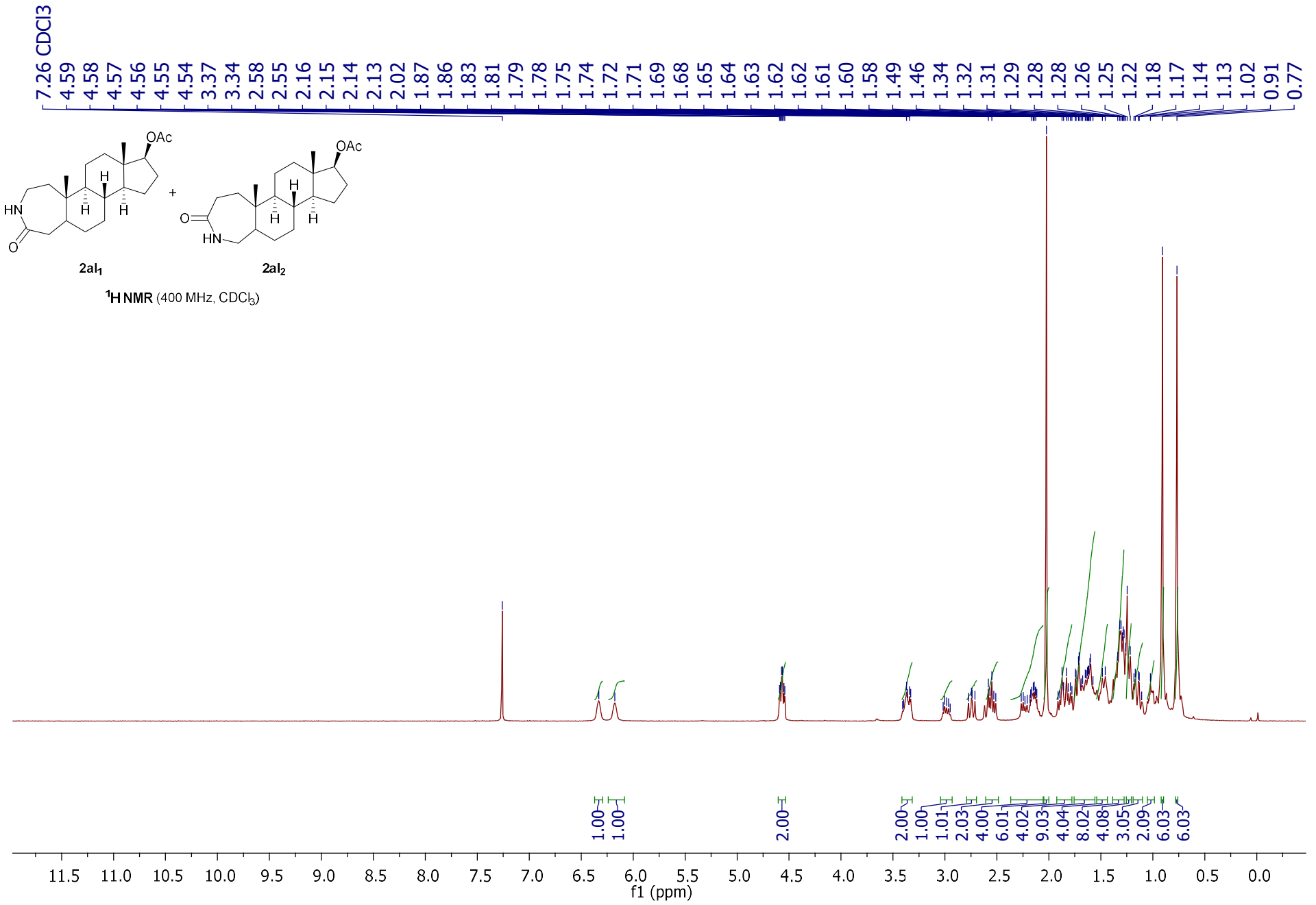
^{13}**C NMR** (101 MHz, DMSO-d_6)

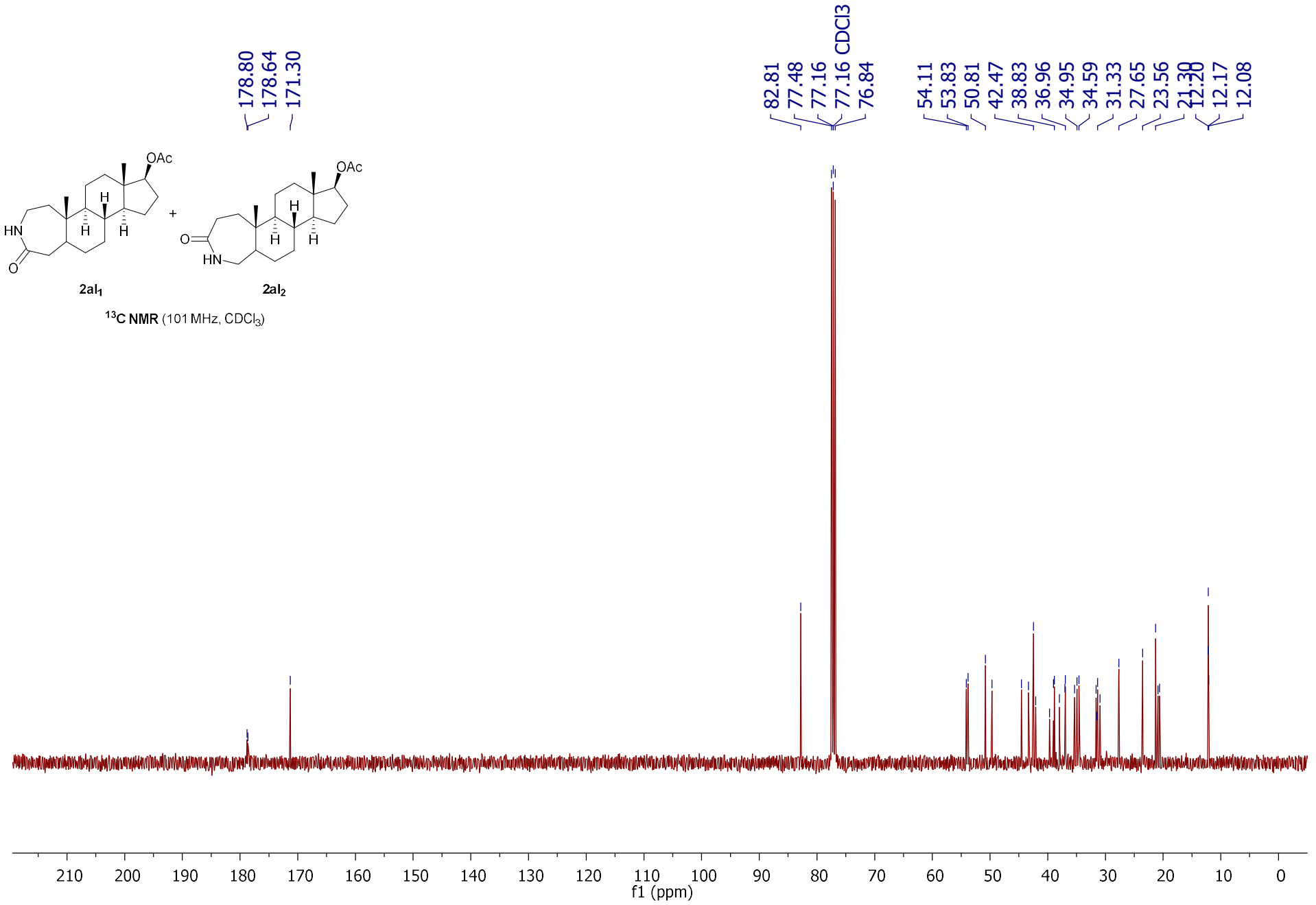


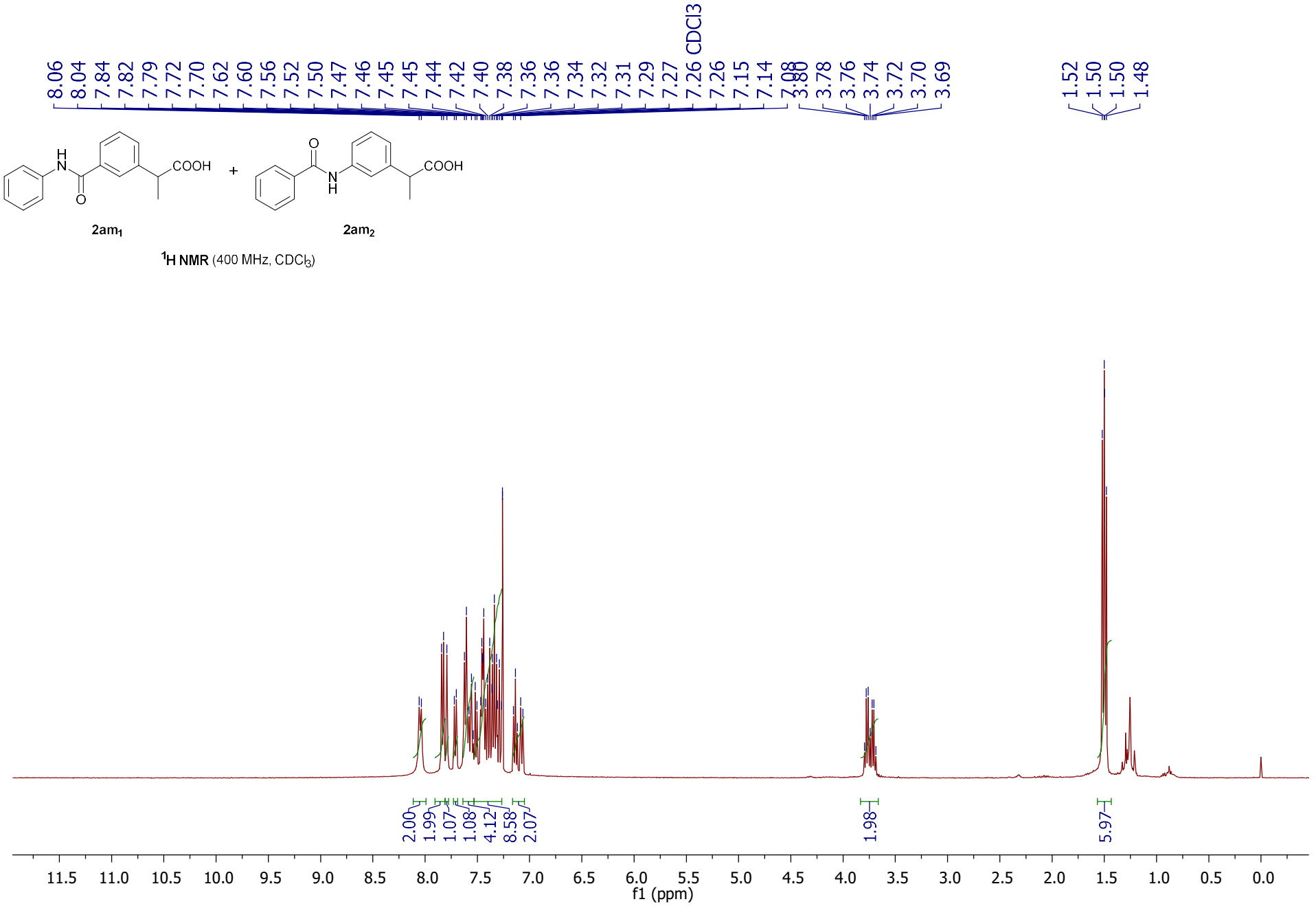
2ak

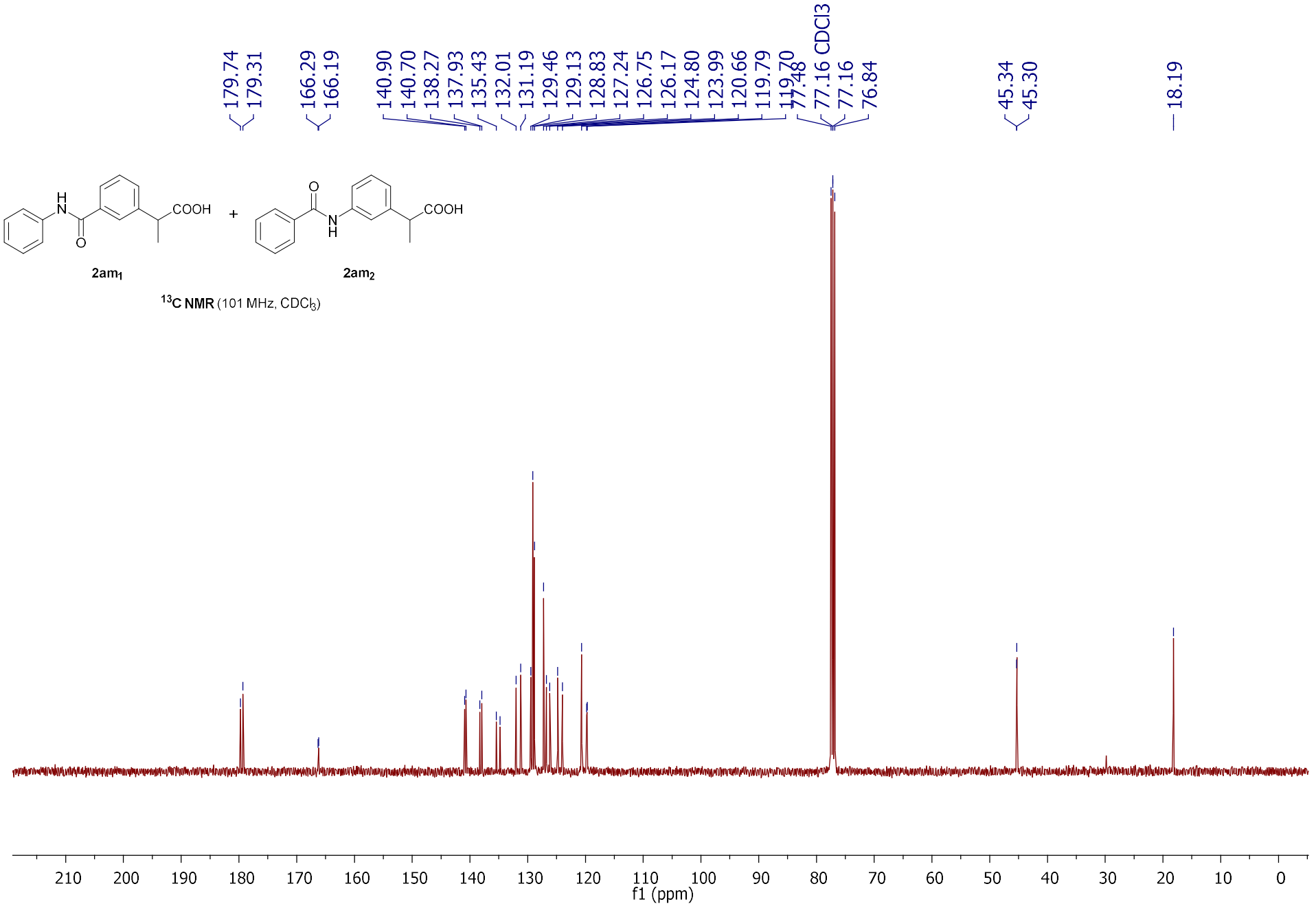
^{1}H NMR (400 MHz, DMSO-d_6)

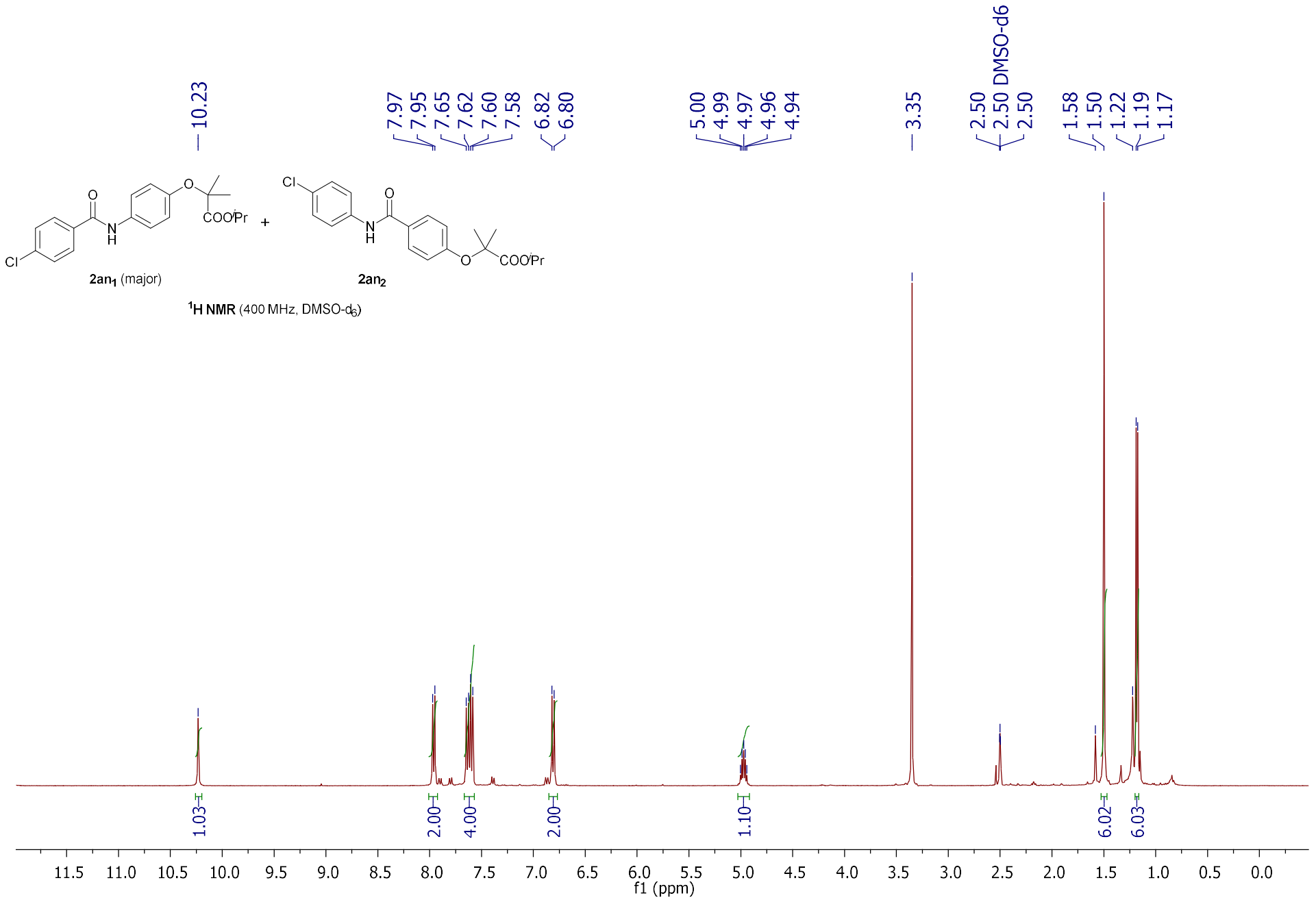

HN
O
HN
H
H
H
O
2ak
^{13}C NMR (101 MHz, DMSO-d$_6$)
168.95
168.18
159.33
119.41
58.18
52.93
51.71
43.93
42.83
42.01
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
36.87
35.54
35.47
35.17
33.24
27.18
23.15
22.74
20.96
12.12
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

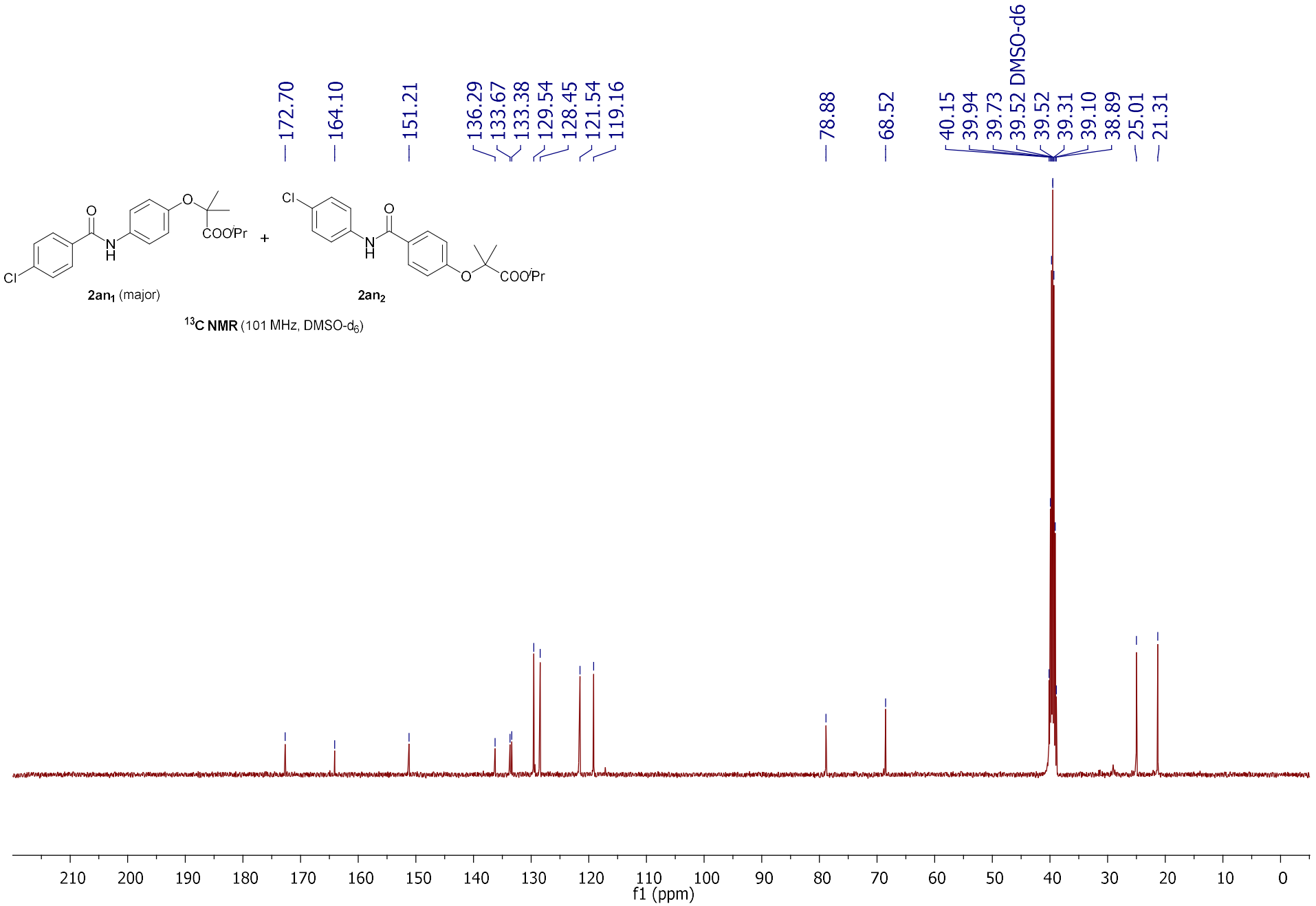

7.26 CDCl3
4.59 4.58 4.57 4.56 4.55 4.54 3.37 3.34 2.58 2.55 2.16 2.15 2.14 2.13 2.02 1.87 1.86 1.83 1.81 1.79 1.78 1.75 1.74 1.72 1.71 1.69 1.68 1.65 1.64 1.63 1.62 1.62 1.61 1.60 1.58 1.49 1.46 1.34 1.32 1.31 1.29 1.28 1.28 1.26 1.25 1.22 1.18 1.17 1.14 1.13 1.02 0.91 0.77
OAc
H
HN
H
H
O
+
OAc
H
O
H
H
HN
2al1
2al2
1H NMR (400 MHz, CDCl3)
1.00 1.00 2.00 2.00 1.00 1.01 2.03 4.00 6.01 4.02 9.03 4.04 8.02 4.08 3.05 2.09 6.03 6.03
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


178.80
178.64
171.30
82.81
77.48
77.16
77.16 CDCl3
76.84
54.11
53.83
50.81
42.47
38.83
36.96
34.95
34.59
31.33
27.65
23.56
21.30
12.20
12.17
12.08
OAc
HN
O
H
+
OAc
O
HN
H
2al1
2al2
13C NMR (101 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.06
8.04
7.84
7.82
7.79
7.72
7.70
7.62
7.60
7.56
7.52
7.50
7.47
7.46
7.45
7.45
7.44
7.42
7.40
7.38
7.36
7.36
7.34
7.32
7.31
7.29
7.27
7.26 CDCl3
7.26
7.15
7.14
7.08
3.80
3.78
3.76
3.74
3.72
3.70
3.69
1.52
1.50
1.50
1.48
COOH
+
COOH
2am1
2am2
1H NMR (400 MHz, CDCl3)
2.00
1.99
1.07
1.08
4.12
8.58
2.07
1.98
5.97
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

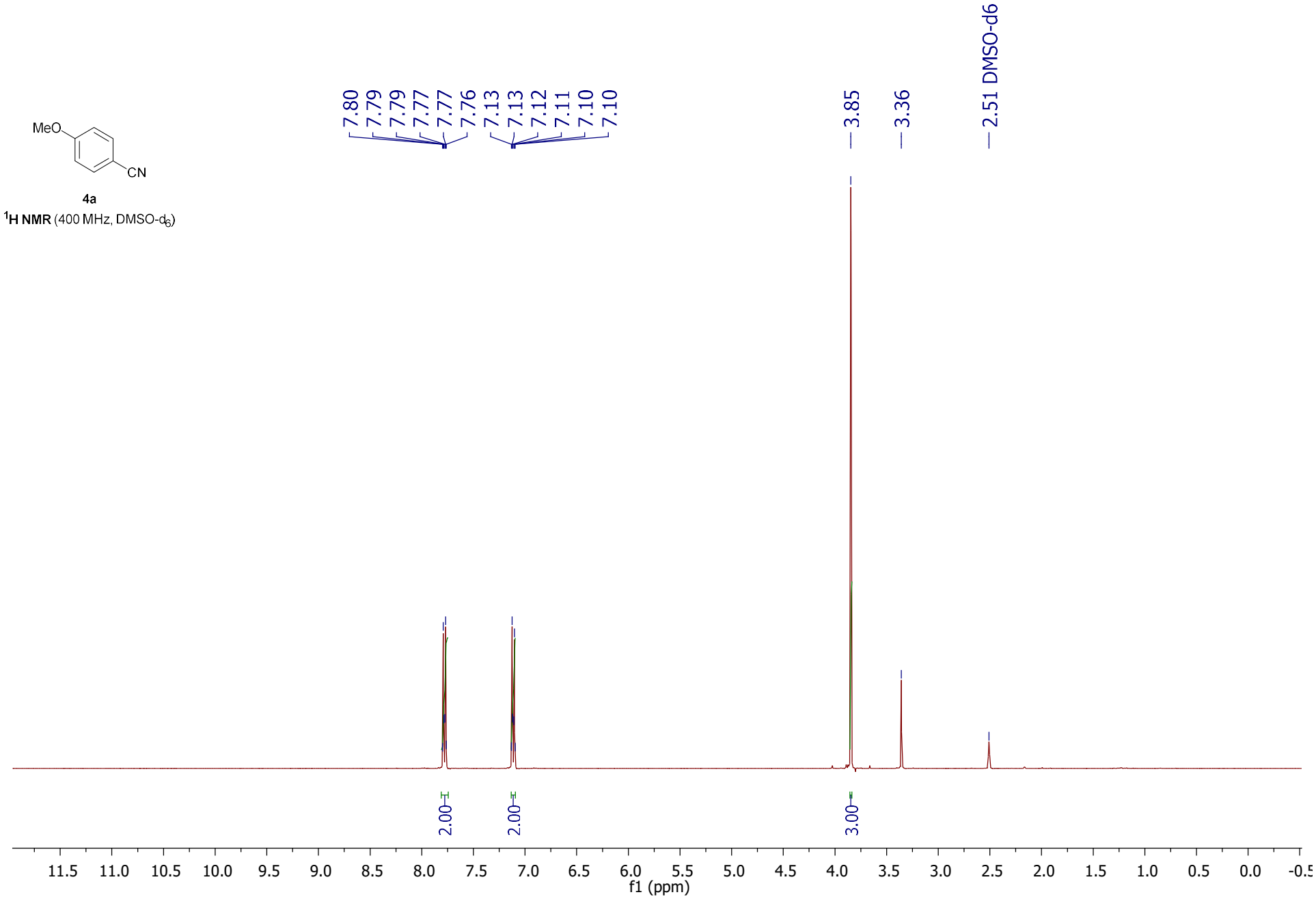

179.74
179.31
166.29
166.19
140.90
140.70
138.27
137.93
135.43
132.01
131.19
129.46
129.13
128.83
127.24
126.75
126.17
124.80
123.99
120.66
119.79
119.70
77.48
77.16 CDCl3
77.16
76.84
45.34
45.30
18.19
COOH
+
COOH
2am1
2am2
13C NMR (101 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

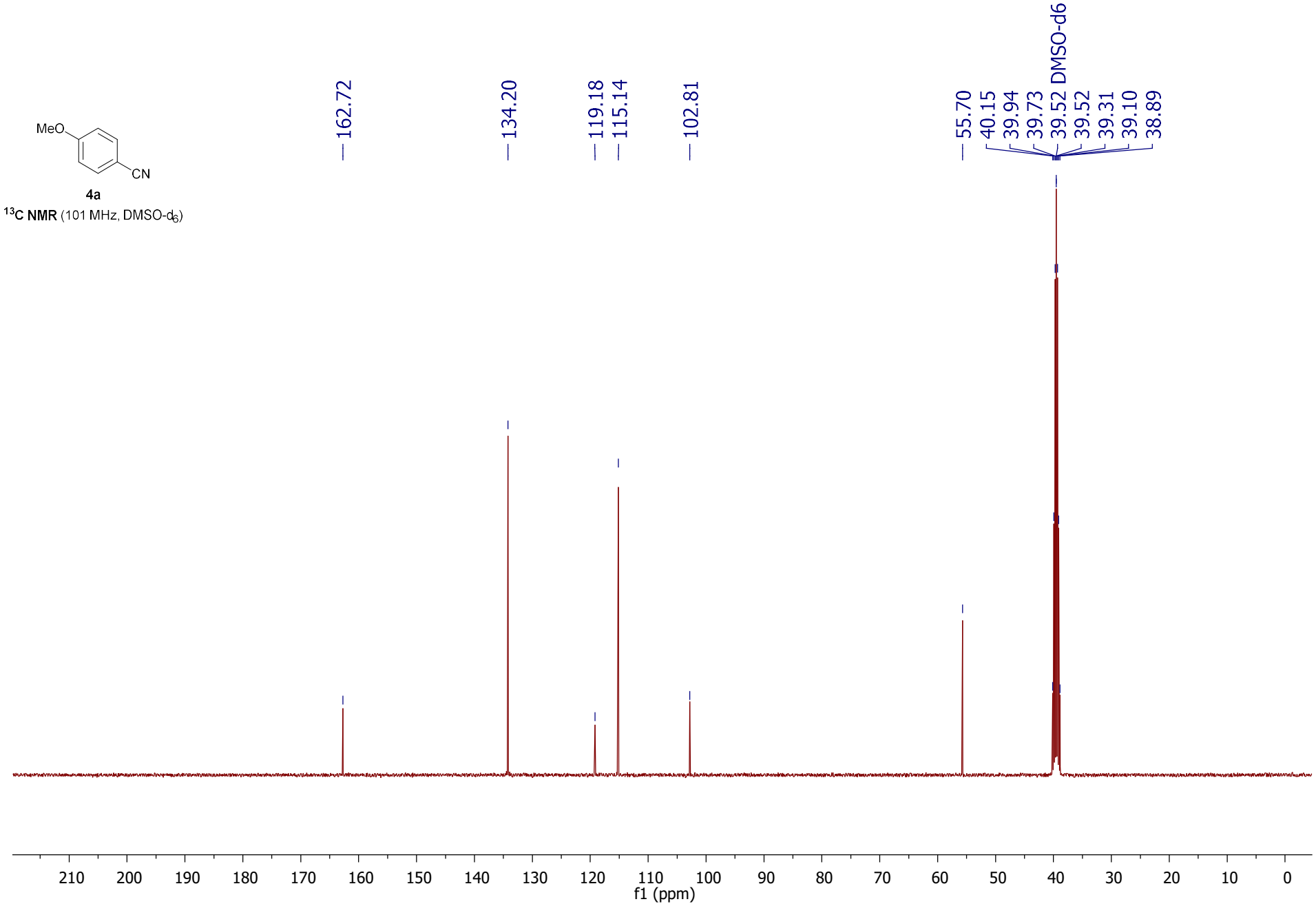

10.23
7.97
7.95
7.65
7.62
7.60
7.58
6.82
6.80
5.00
4.99
4.97
4.96
4.94
3.35
2.50
2.50 DMSO-d6
2.50
1.58
1.50
1.22
1.19
1.17
Cl
O
N
H
O
COO'Pr
+
Cl
O
N
H
O
COO'Pr
2an1 (major)
2an2
1H NMR (400 MHz, DMSO-d6)
1.03
2.00
4.00
2.00
1.10
6.02
6.03
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

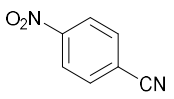


2an$_1$ (major) **2an$_2$**

^{13}**C NMR** (101 MHz, DMSO-d$_6$)

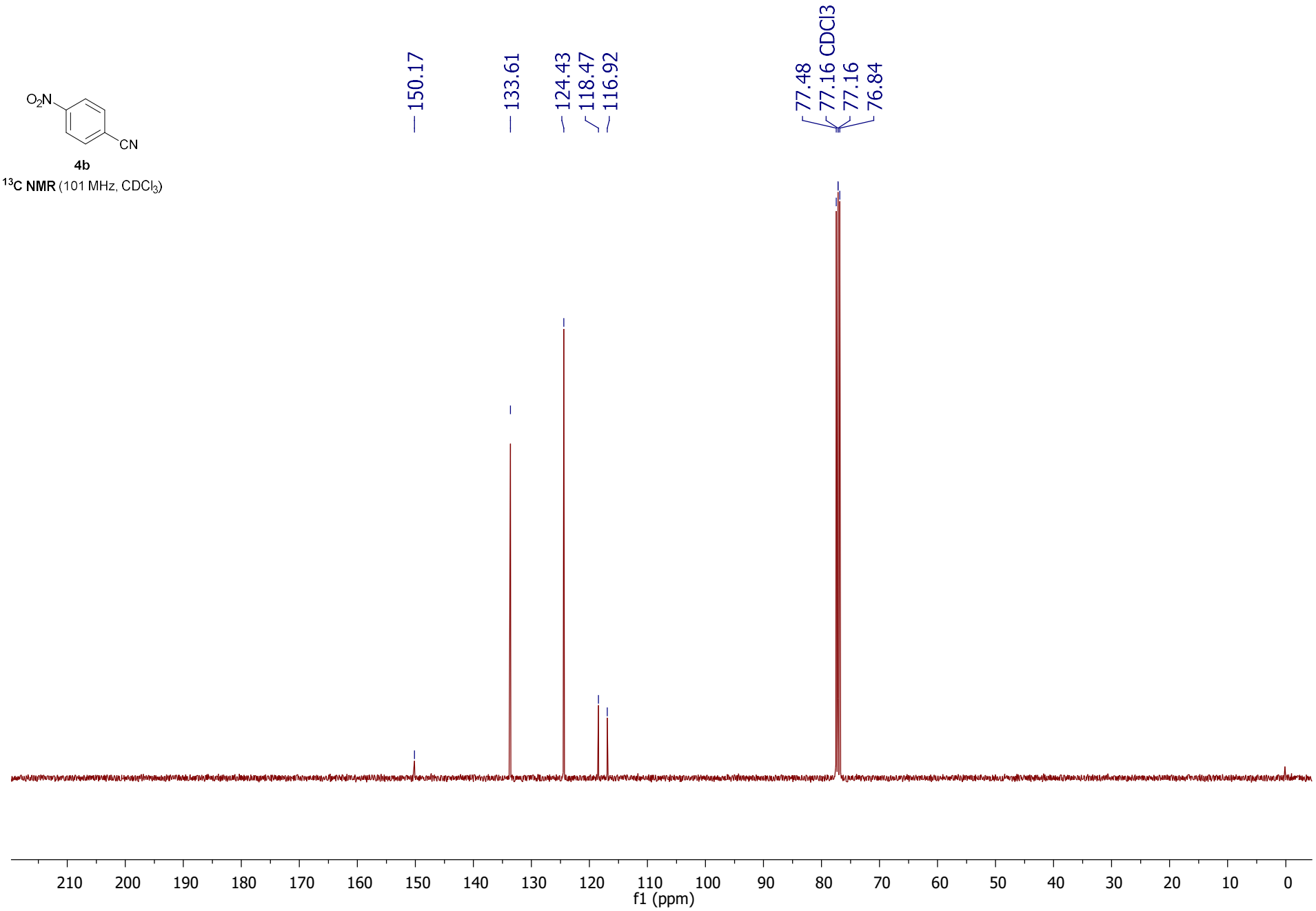

MeO
CN
4a
1H NMR (400 MHz, DMSO-d6)
7.80
7.79
7.79
7.77
7.77
7.76
7.13
7.13
7.12
7.11
7.10
7.10
3.85
3.36
2.51 DMSO-d6
2.00
2.00
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

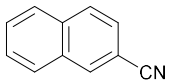

MeO
CN
4a
13C NMR (101 MHz, DMSO-d6)
162.72
134.20
119.18
115.14
102.81
55.70
40.15
39.94
39.73
39.52 DMSO-d6
39.52
39.31
39.10
38.89
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



4b

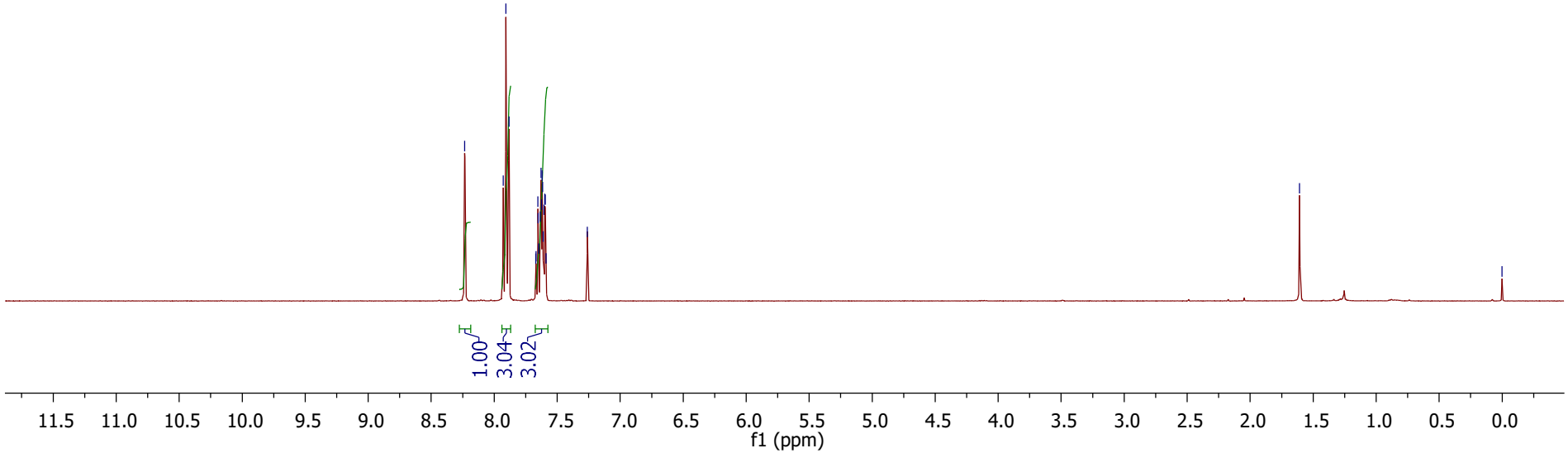
^{1}H NMR (400 MHz, $CDCl_3$)

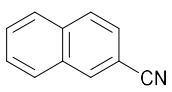

O2N
CN
4b
13C NMR (101 MHz, CDCl3)
150.17
133.61
124.43
118.47
116.92
77.48
77.16 CDCl3
77.16
76.84
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



4c

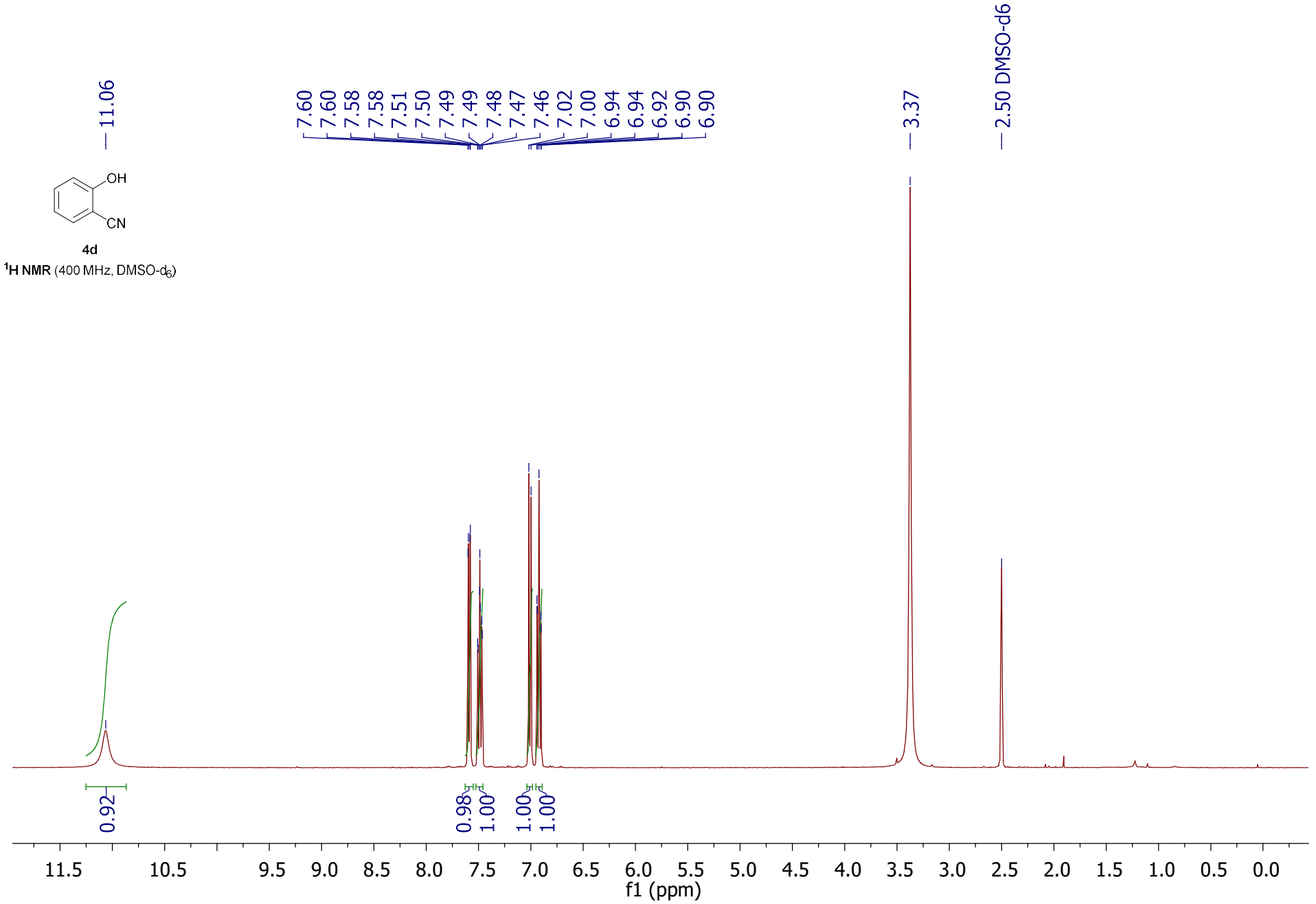
^{1}H NMR (400 MHz, $CDCl_3$)

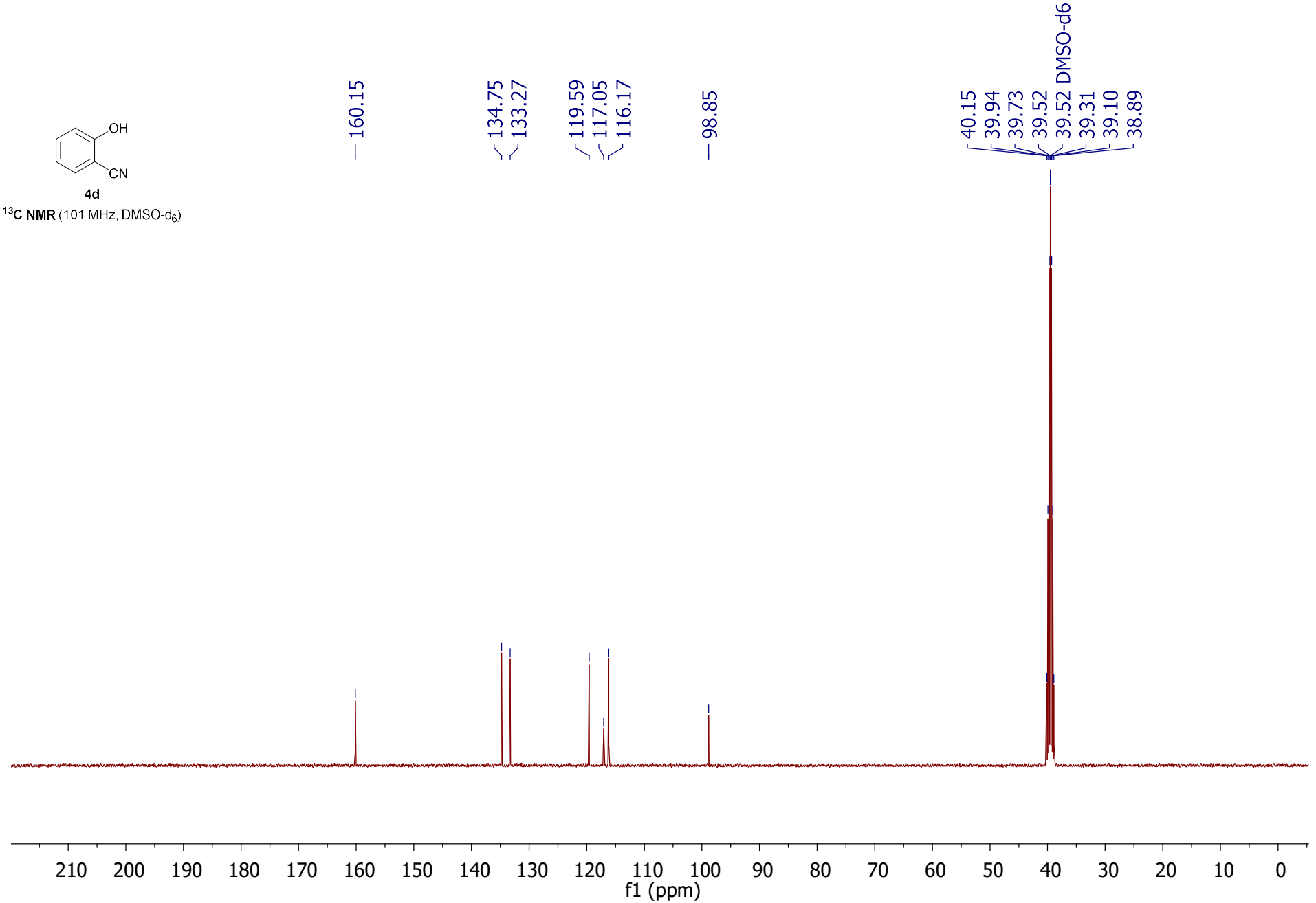


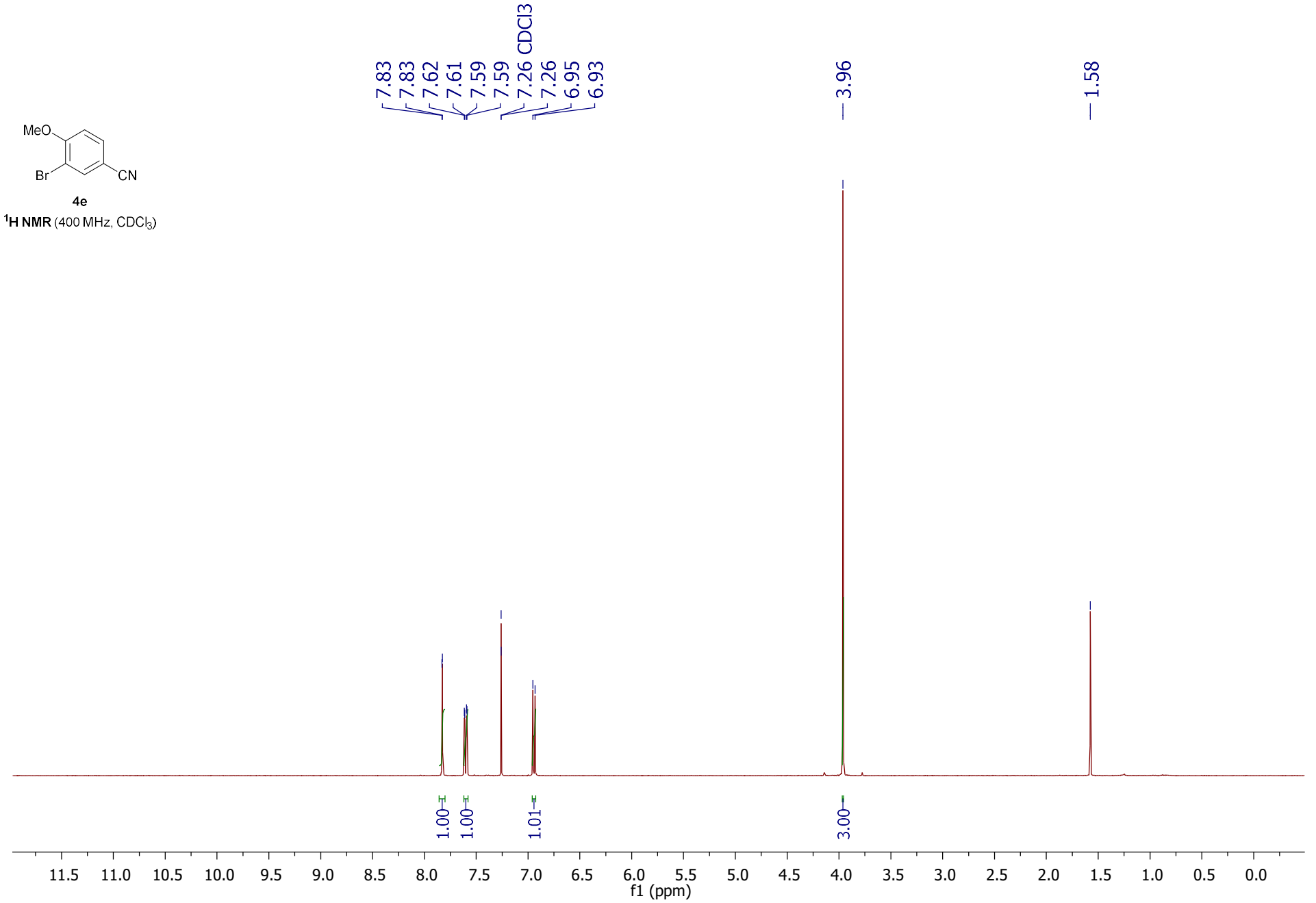


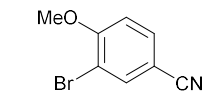
4c

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


11.06
7.60
7.60
7.58
7.58
7.51
7.50
7.49
7.49
7.48
7.47
7.46
7.02
7.00
6.94
6.94
6.92
6.90
6.90
3.37
2.50 DMSO-d6
OH
CN
4d
1H NMR (400 MHz, DMSO-d6)
0.92
0.98
1.00
1.00
1.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OH
CN
4d
13C NMR (101 MHz, DMSO-d6)
160.15
134.75
133.27
119.59
117.05
116.17
98.85
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

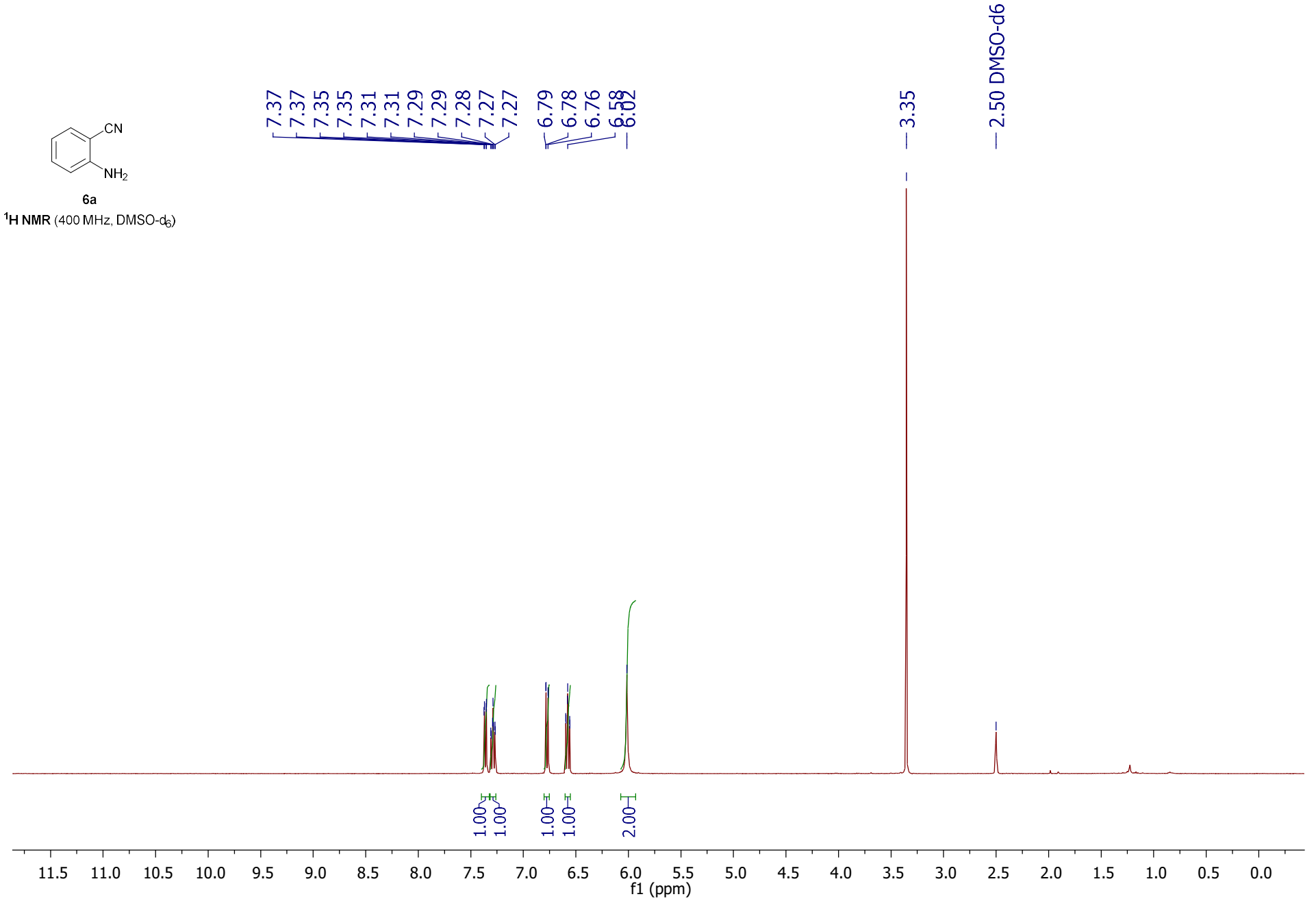

MeO
Br
CN
4e
1H NMR (400 MHz, CDCl3)
7.83
7.83
7.62
7.61
7.59
7.59
7.26 CDCl3
7.26
6.95
6.93
3.96
1.58
1.00
1.00
1.01
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

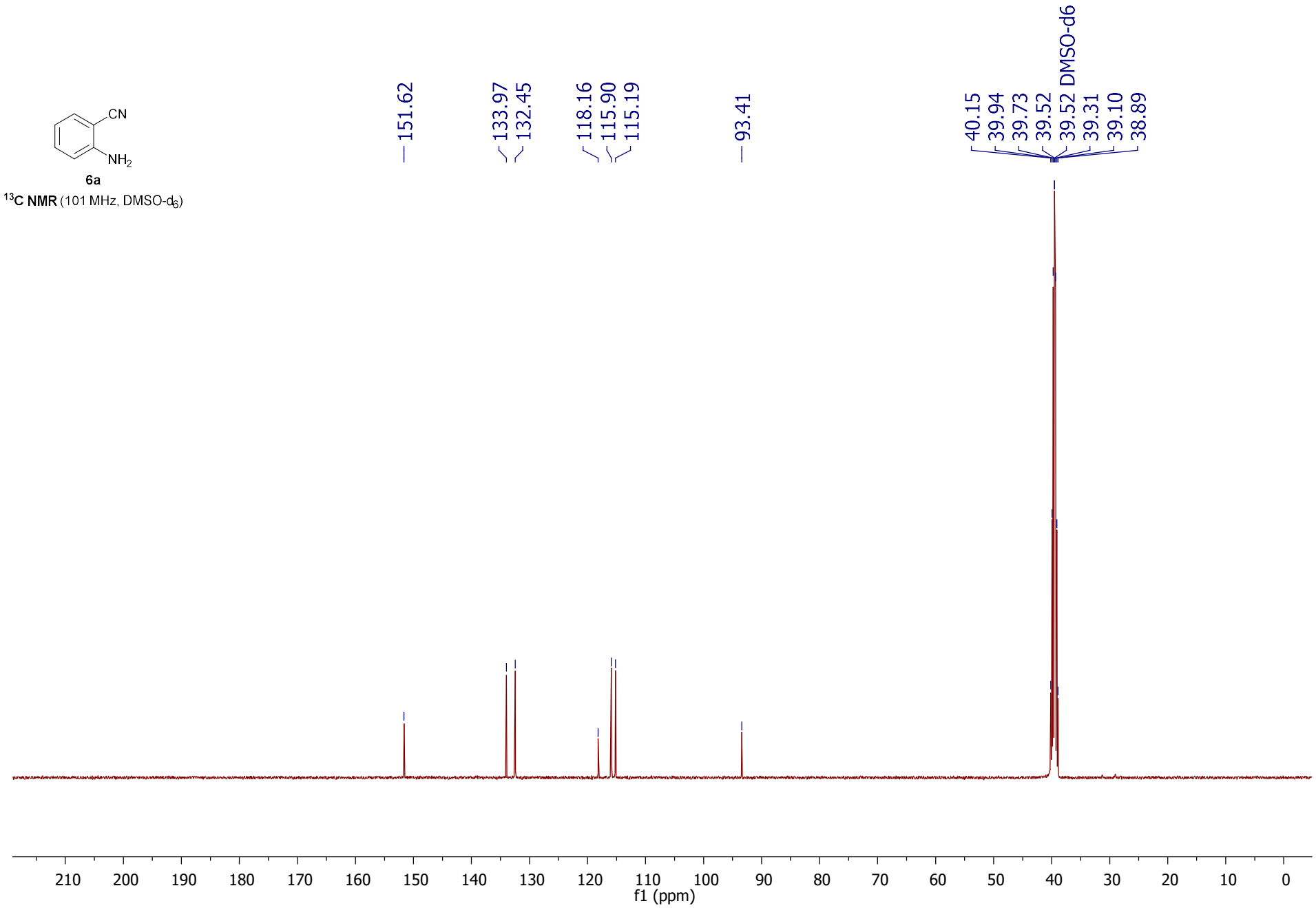


4e

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

159.57
136.83
133.31
117.90
112.47
112.03
105.38
77.48
77.16
77.16 CDCl3
76.84
56.71


CN
NH2
6a
1H NMR (400 MHz, DMSO-d6)
7.37
7.37
7.35
7.35
7.31
7.31
7.29
7.29
7.28
7.27
7.27
6.79
6.78
6.76
6.58
6.02
3.35
2.50 DMSO-d6
1.00
1.00
1.00
1.00
2.00
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


CN
NH2
6a
13C NMR (101 MHz, DMSO-d6)
151.62
133.97
132.45
118.16
115.90
115.19
93.41
40.15
39.94
39.73
39.52
39.52 DMSO-d6
39.31
39.10
38.89
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)